Exhibit 30

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF NEW YORK

IN RE: ACETAMINOPHEN ASD-ADHD PRODUCTS LIABILITY LITIGATION	)	MDL No. 3043
	)	Case No. 1:22-md-03043-DLC
THIS DOCUMENT RELATES TO: All Cases, 1:22-MD-03043	)	JUDGE DENISE COTE

MONDAY, AUGUST 28, 2023

CONFIDENTIAL - PURSUANT TO PROTECTIVE ORDER

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Videotaped Deposition of CRAIG POWELL, M.D. Ph.D., taken pursuant to notice and conducted at the offices of Butler Snow, 1819 5th Avenue N., Suite 1000, Birmingham, Alabama, commencing at 8:31 a.m., Central Time, on the above date, before Jennifer A. Dunn, Registered Merit Reporter, Certified Realtime Reporter; California, Illinois & Texas Certified Shorthand Reporter, and Missouri Certified Court Reporter.

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Lisa Qian

I N D E X

E X H I B I T S

E X H I B I T S (Cont.)

E X H I B I T S (Cont.)

P R O C E E D I N G S

(Monday, August 28, 2023 at 8:31 a.m., Central Time.)

THE VIDEOGRAPHER: We are now on the record. My name is Jeff Fleming. I'm a videographer for Golkow Litigation Services.

Today's date is August 28th, 2023. The time is 8:31 a.m.

This video deposition is being held in Birmingham, Alabama, in the matter of Acetaminophen/Tylenol, ASD-ADHD, Products Liability Litigation.

The deponent is Dr. Craig Powell.

Appearances will be noted on the stenographic record.

Our court reporter is Jennifer Dunn and will now swear in the witness.

CRAIG POWELL, M.D., Ph.D.,

of lawful age, having been first duly sworn to tell the truth, the whole truth and nothing but the truth, deposes and says on behalf of the Plaintiffs, as follows:

EXAMINATION

BY MS. HUNT:

Q Good morning, Dr. Powell.

A Good morning, Ms. Hunt.

Q I understand you've been deposed previously; is

that right?

A Yes, a few times.

Q Okay.

A A handful.

Q I'm sorry, go ahead.

A I said a handful. I don't know.

Q Okay. So I won't bore you with all the rules for a deposition. I know you're assisted by able counsel, but there are a few things I want to emphasize before we get started.

It's not an endurance test. So if you need a break, please let us know. I would just ask that you answer any question pending and then I'm happy to take a break any time.

Your counsel is going to object, I'm sure, probably more than once during this deposition. Unless he instructs you not to answer, you still have to answer the question.

If you don't understand the question I'm asking, please ask me to clarify and I'll be happy to do it. I don't want you to answer something and then tell me later you didn't understand; is that fair?

A Yes, ma'am.

Q Okay. And do you understand the oath that you just swore is the same oath that would be administered in a

courtroom?

A Yes, I do.

Q And you're under oath exactly like you would be in a court of law?

A Yes, I understand.

Q Okay. Did you bring anything with you today?

A I brought some snacks, some water, and a TopoChico, but I have the -- some of the papers that are -- I referenced, and a copy of my report and a few other things, but nothing that you don't have a copy of.

Q Okay. Are there any notes or other types of annotations anywhere in those documents?

A Not to my knowledge.

Q Okay. I want to look at what's been marked as Exhibit 200.

(Powell Deposition Exhibit 200 marked for identification.)

BY MS. HUNT:

Q Dr. Powell, this is your Notice of Deposition. Have you seen this document before?

A I have.

Q And are you aware that there were document requests attached at the back as Schedule A?

A I'm aware that there were document requests, yes.

Q Okay. I only want to talk about a few of them,

specifically requests 6 and 7, which are on page -- if you look in the top right-hand corner, it should say "200.7."

A Mm-hmm. Got it.

Q Okay. So these requests both relate to communications with specific third parties about the topics that you address in your report.

And I'd like to understand a little bit about your efforts to respond to these requests.

Did you do an e-mail search for all these names?

A No. Because I haven't communicated with any of the names in part 6.

Q Do you know any of them?

A I've heard of Eric Fombonne. I've heard of Terrie Inder. I don't know if I know who Anthony Scialli is.

I'm probably confusing him with Anthony someone else. And that's all.

Q Okay.

MR. PADGETT: Amanda, just real quickly.

Will you have copies of the hard copies?

MS. HUNT: Of the exhibits?

MR. PADGETT: Yeah.

MS. HUNT: I thought we gave you a copy.

MR. PADGETT: Oh, never mind. Got it.

BY MS. HUNT:

Q Okay. And as part of your -- forming your

opinions in this case, did you contact the authors or any of the researchers involved in the studies you reviewed?

A I don't believe so, no.

Q Okay. And for request number 7, do you know any of the people listed in that request?

A Not that I'm aware of, no.

Q Okay. All right.

I'd like to move to the next page. So that's 200.8, and I want to take a look at request 11, 12 and 13.

Let me ask you this: You've never conducted any experiments using acetaminophen; is that fair?

A I don't think I've ever administered acetaminophen and done an experimental condition.

Q Okay.

A That I can recall.

Q Could you have done a preclinical experiment using acetaminophen as part of your work in this case?

MR. PADGETT: Object to form.

THE WITNESS: As part of my work in this case, I would say no.

Could I have done such an experiment? Yes.

BY MS. HUNT:

Q Okay. So you have the equipment that you would need?

A I have access to it, yes.

Q Okay. And do you have any plans to conduct a preclinical experiment with acetaminophen?
A Not as we sit here today, no, ma'am.
Q And the lawyers for the manufacturers of acetaminophen haven't asked you to do that?
MR. PADGETT: Object to form.
THE WITNESS: No one has asked me to do that.
BY MS. HUNT:
Q Okay. And in putting together your expert report, were you given access to any unpublished neurotoxicology data from Johnson & Johnson or any other acetaminophen manufacturer?
A Not to my knowledge.
Q To your knowledge, has Johnson & Johnson ever conducted a neurotoxicology study on acetaminophen?
A I don't know.
Q Okay. Would you want to know that?
A Not to form the opinions I put in my report, no, ma'am.
Q Okay. Do you think that preclinical testing for endpoints like neurotoxicity should be required before a drug is given to pregnant women?
A I'm not sure I have an opinion on that.
Q Okay. So you'd be fine with it either way?
A With what either way? I'm sorry.

Q With administering a drug to pregnant women whether it had undergone that preclinical evaluation or not?

MR. PADGETT: Object to form.

THE WITNESS: Sorry. I think that would depend on the drug and the context.

BY MS. HUNT:

Q Okay. And I know that you take issue with the statistical methods employed by some of the researchers in this case, and we're going to talk about that, but as part of your analysis, did you rerun any of their data?

A I did not.

Q Okay. And as you were going through the expert reports of Dr. Pearson and Dr. Cabrera, are you familiar with the fact that they scored or otherwise weighted the studies that they reviewed?

A I'm aware that Dr. Pearson made up a scoring system and applied it without defining how to apply it. And I'm aware that Dr. Cabrera talked about it, weight of the evidence, and I don't think he scored it with a number.

Q Okay.

A To the best of my recollection.

Q You didn't try to go through and rescore the studies yourself?

A I did a weight of -- I did a systematic review of the evidence and in doing so I considered many factors and

as -- at least two of the experts on the plaintiffs' side, for the plaintiffs, noted that putting a score is not necessary for -- even for a weight of the evidence evaluation.

So, no, I didn't add a number.

Q Okay. And I'm not criticizing you.

A I understand.

Q I'm just trying to figure out the universe of information that might exist.

A Understood.

Q That's why we're talking about this notice.

A Mm-hmm.

Q So is it fair to say that you -- I know you disagree with it, but you understood the weighting or the scoring in Dr. Pearson and Dr. Cabrera's reports, you just chose a different approach?

A I have to say no to that.

Q Okay. We'll talk about that more later today.

Going back to the notice. Request number 16 concerns your invoices and time records.

And I noticed in looking at your invoices that they only cover time up until June.

Is that because you haven't invoiced since June?

A I don't have an invoice since June that I've submitted.

Q Okay. Have you been paid for your time since June?

A Some of it. The time that I spent on this case, yes.

Q Okay. How did you get paid without the invoice?

A Oh, I'm sorry. I haven't been -- I may have misspoke.

I have not been paid anything in this case actually to date.

Q Okay.

A Sorry.

Q Okay. So there -- there is no invoice floating around for the time between June and now?

A I have not finalized an invoice and submitted it for the time between June, no.

Q Okay. Do you have a rough idea of how many hours you've put in in that time?

A I don't -- I don't. I can tell you that total time I've spent is probably about 40 to 45 eight-hour days' worth of time, my vacations, nights and weekends.

Q 40 to 45 eight-hour days. Okay. All right.

I'd like to turn now to what has been marked as Exhibit 203.

(Powell Deposition Exhibit 203 marked for identification.)

BY MS. HUNT:

Q Dr. Powell, this is a copy of the CV you provided when you served your initial report, and I just want to check and see that it's up to date.

Is there anything that you would need to add?

A There's maybe a couple papers that I haven't added to my academic CV, and I -- I am named as a coinvestigator on a Neuren Pharmaceuticals, or Neuren Incorporated funded human participant study in the Civitan International Research Center which I direct.

Those funds are supporting a clinical -- a phase, I guess it's Phase II or I, clinical trial, of a novel -- new investigational drug for a specific genetic form of autism and intellectual disability.

I don't receive any part of my salary from that grant, and my understanding of my role is I'm there as a neurologist who can, if need be, if there's something that comes up on any of the scans or any medical issues, then I can help the patients get to where they need to go.

Q Okay. And I think we found three additional studies from 2022 and 2023 that were not on your CV.

Does that sound about right to you? I think you said --

A I don't know.

Q -- maybe a handful. Okay.

A That sounds like a little more than what I would have guessed.

Q I've got one where the lead author is Breen. Are you familiar with that study?

A Who's the last author, or do you know the title of that study?

Q I would be happy to pull it.

A Thanks.

Q And I think actually Dr. Cullison is a co-author on this paper.

Dr. Powell, are you aware that he is also a testifying expert in this case?

A I've been made aware of that, yes.

Q And have you ever talked to him about this case?

A No, I haven't.

Q Okay.

A I'm glad you pointed this out. I don't --

Q Can you confirm that this is, in fact, you?

A This is I. And, yes. I am on this paper --

Q Okay.

A -- as part of the Developmental Synaptopathies Consortium, yes.

Q Okay. Great.

All right. Moving on to the exhibit that's been marked as 201.

(Powell Deposition Exhibit 201 marked for identification.)

BY MS. HUNT:

Q Dr. Powell, does this appear to you to be a redline of the amended expert report you submitted against the original expert report you submitted?

A Yes.

Q Okay. And under the Federal Rules of Civil Procedure, you understand that your expert report has to have a complete statement of all your opinions?

MR. PADGETT: Object to form.

THE WITNESS: I am not aware of any of the statutes regarding the -- what my report needs to contain or not contain, to be perfectly honest.

BY MS. HUNT:

Q Okay. Well, are all your opinions in this expert report related to this case?

A I would say that --

MR. PADGETT: Object to form.

THE WITNESS: I would say that my opinions on the tasks put before me are in this report, and I have additional opinions that weren't part of my task.

BY MS. HUNT:

Q Okay. So I'm talking specifically about your opinions as they relate to this lawsuit.

Are all of those opinions in this expert report?

MR. PADGETT: Object to form.

THE WITNESS: Again, all of the opinions that I was asked to provide on the rodent animal literature, where -- about acetaminophen and potential nervous system consequences are in this report.

And, you know, as a scientist and a physician, I have my own opinions from additional literature that I've read that aren't in this report, that weren't part of my task.

BY MS. HUNT:

Q What are the opinions that you have that aren't in this report about acetaminophen and neurodevelopment?

MR. PADGETT: Object to form.

THE WITNESS: I'm not sure I can answer that question. It's too broad.

If you can narrow it down, I'd be happy to answer.

BY MS. HUNT:

Q What about that question do you not understand, Dr. Powell?

A I understood the question. It's too broad for me to give an answer.

Q Okay. So you can't say, sitting here today, how many other opinions you have about acetaminophen in

neurodevelopment?

A I haven't enumerated in my mind how many different opinions I have about acetaminophen, but I'm happy to answer any questions about specific opinions --

Q Okay.

A -- that I might or might not have.

Q I'm talking about acetaminophen in neurodevelopment specifically.

A Me too.

Q Okay. And so do you understand that we're entitled under the -- under the Rules of Civil Procedure to know the full scope of your opinion that you're going to offer at trial?

MR. PADGETT: Object to form.

THE WITNESS: I don't, but I understand that this deposition is meant to uncover any and all opinions that I have.

MS. HUNT: Okay. I'll just say that to the extent that Dr. Powell's going to offer opinions outside of what's included in his Rule 26 report, we're going to reserve our right to re-depose him at that time.

BY MS. HUNT:

Q Do you understand that your report is also --

MR. PADGETT: I'll -- I'll -- I'll object to

that.

The opinions that he's setting forth for this case are in the report. Just to make that crystal clear.

BY MS. HUNT:

Q Okay. And you may not understand this, but under the Federal Rules, your report also has to include the facts and data considered by you in forming your opinion.

Did you list all of those facts and all that data in your Materials Considered List?

A I listed --

MR. PADGETT: Object to form.

THE WITNESS: I listed everything that I used to form my opinion based on the specific task that I was given, which was to review the rodent literature on acetaminophen and potential downstream consequences.

BY MS. HUNT:

Q Okay. Is there anything you've considered in forming your opinion that's not on your Materials Considered List?

A All I will say is that I've read additional literature that's not in this, so that I understood the context of what I -- the job that I was doing.

So -- but the basis of my opinion in the report, I've cited everything that I used. I think there may be --

I produced one more paper, Tyl 2009, that I haven't referenced in my report.

Q Okay. So I'm trying to understand your answer.

There's additional literature that you considered in order to understand the job you were doing; is that fair?

A To understand the context, yes.

Q Okay. And that -- that literature is not on your Materials Considered List?

A Correct. Because it wasn't part of my task in this case.

Q Does your counsel have access to the list of what that literature might be?

A I don't know, probably, but it's -- I don't have -- I don't list it. I mean, I looked at some of the epidemiologic studies, for example, just to get an idea of what was out there.

Q Okay. Okay. We can talk about that more in a little bit.

Do you understand that this case concerns claims brought on behalf of women and their children who claim injuries as a result of exposure to acetaminophen?

A I know it's a class action suit and there are people involved as plaintiffs.

Q Okay. What do you understand the claims in this case to be?

A My understanding is there's a claim that acetaminophen, or acetaminophen-containing products are alleged to increase the risk for autism spectrum disorder and/or attention deficit hyperactivity disorder.

Q Okay. Do you feel like you had enough time to come to the opinions you expressed in the expert report you tendered?

MR. PADGETT: Object to form.

THE WITNESS: I would say that I would have -- I always would love to have more time to review the literature because that's what I do for a living, but I'm pretty comfortable with my opinions in my report.

BY MS. HUNT:

Q Okay. And do you understand that we're also entitled to know, in addition to knowing your opinions, the bases for your opinions in this case?

MR. PADGETT: Object to form.

THE WITNESS: Again, I -- you've mentioned that, and as I said, all of the things that I relied upon primarily to come to these opinions in my report are listed in the reference section.

MS. HUNT: Okay.

THE WITNESS: With one exception, which is after those opinions were made, I have reproduced the

Tyl 2009 paper.

MS. HUNT: Okay.

MR. PADGETT: It's on there.

MS. HUNT: Yeah, I saw it.

BY MS. HUNT:

Q Do you hold any opinions about the conduct of Johnson & Johnson or any other manufacturer of acetaminophen in whether their conduct was proper or not?

A I do not.

MR. PADGETT: Object to form.

BY MS. HUNT:

Q Okay. All right. Turning to your report.

I want to talk to you a little bit about your work outside of the context of litigation.

So you say on page 1 of your expert report: "I've spent more than 20 years working with genetically-modified laboratory animals to study their developmental disorders."

Did I read that reasonably correct?

MR. PADGETT: I'll object to form. Just recurring objection that this is not -- this is the redline, that's at 201, as opposed to the actual amended report.

MS. HUNT: Okay. You can have a standing objection.

BY MS. HUNT:

Q So, Dr. Powell, is it fair to say that most of your career has been focused on creating and manipulating genetic mass models of autism?

A I would say more than half of my research in the last 20-plus years has been in some way related to that. Certainly not all.

Q Right. Right. I understand that, and we'll talk about some of your other work in just a little bit.

But is the goal of that work to study potential interventions for people with autism?

A In part. The goal of that work is to take known causes of autism, most of the time, in humans, and recapitulate those, to some degree, in an animal model, genetic animal model, and then we try to understand, using a variety of techniques, what might be changed about the brain's function and whether or not those changes have any relevance or any behavioral change in the animal model, which we hope might some day be demonstrated to be relevant to the human disorder in a specific genetic cause or across ASD at large.

Q Okay. And I'd like to talk a little bit about why it might be helpful to do that in an animal model.

Is it fair to say that animals can have a lot of the same biological processes and systems that humans do?

MR. PADGETT: I think I would say it's fair to say that some of the systems overlap with humans and it's mostly unknown to what extent that happens and that the vast majority of findings in animal models don't translate to humans in neuropsychiatric disorders, particularly uniquely human disorders, that are behaviorally defined, such as autism spectrum disorder and ADHD.

BY MS. HUNT:

Q So do you feel that most of your own work in mice is never going to translate to humans?

MR. PADGETT: Object to form.

THE WITNESS: I would say that my hope is that anything that we find in mice will translate to humans. And we've made attempts to do so.

BY MS. HUNT:

Q And obviously mice are different than humans and obviously rats are different than humans, but both of those species have, for example, an endocannabinoid system, right?

A That's my understanding, yes.

Q Okay. And they both have endocrine systems, correct?

A Yes.

Q Okay. Can rodents experience oxidative stress?

MR. PADGETT: Object to form.

THE WITNESS: You'd have to define oxidative stress. I agree with Dr. Pearson's statement that it's a very, very diffuse and vague concept, oxidative stress. Depends on what you mean.

BY MS. HUNT:

Q So sitting here today, you don't know if rodents can experience oxidative stress?

A That's not my answer. My answer is: I don't know what you mean when you say "oxidative stress."

Q Okay. I'm talking about --

A It's a vague and -- I'm sorry.

It's a vague --

Q No. Go ahead.

A -- and diffuse term, as I said, so it's overly broad and ambiguous. So it's hard for me to answer.

If you can define it, I'm happy to answer.

Q Okay. So do you think that rodents can experience an imbalance of reactive oxygen species in their bodies.

A Yes, I do.

Q Okay. Do rodents have the same neurotransmitters that humans might have in their brains?

A Many of them.

Q And is it fair to say that you can control a lot of the variables in animal experiments?

MR. PADGETT: Object to form.

THE WITNESS: I would say that you can control some, but not all.

BY MS. HUNT:

Q Can you control more variables in animal experiments than you can in, for example, an observational human study?

A I would say that's --

MR. PADGETT: Object to form.

THE WITNESS: Generally speaking, that's true.

BY MS. HUNT:

Q So there would be, for example, a lower risk of confounding in an animal experiment?

MR. PADGETT: Object to form.

THE WITNESS: Than in -- I'm not sure what your -- lower than what? I'm sorry.

BY MS. HUNT:

Q A lower risk of confounding than you might see in a human observational experiment?

MR. PADGETT: Same objection.

THE WITNESS: I would say, generally speaking, that's my understanding, yes.

BY MS. HUNT:

Q Would there be a lower risk of misclassification bias in an animal experiment as opposed to a human

observational experiment?

A I would agree with that.

Q Okay. And you can control individual variables in an animal experiment with a lot more precision than you could in a human observational experiment, fair?

A Fair.

MR. PADGETT: Object to form.

THE WITNESS: I would agree.

BY MS. HUNT:

Q And so my understanding is a lot of your work in mice has been related to the Shank3 mutation; is that a fair statement?

A Some of it, but I would -- I mean, some portion of it, but less than half.

Q Okay. A significant amount of your work?

A I mean, I spent 10 years studying Shank3 mouse mutants and published a handful of papers on it, yes.

Q Okay. 10 years is a long time to me.

A Well, I was also looking at other things. I've studied multiple genetic models of autism. More than most.

Q Would you agree with me that in humans autism has a pretty heterogenous presentation?

A Autism spectrum disorder is a spectrum and it has a wide -- a fairly broad range of, I guess, severity of general symptoms and comorbidities.

Q And I think you say -- if we want to turn to page 22 of your report that's been marked as Exhibit 201.

I think you say at the end of that page: "Among ASD researchers, the same goes. If you've seen one child with autism you've seen one child with autism. Meaning that each individual is unique and may, in fact, have unique underlying biology contributing to their ASD."

Do you still agree with that statement?

A The statement -- with the caveat that the term "may" is in there, yes.

Q Okay.

A It's in the realm of possibility, so I have to agree.

Q Okay. And even when there's a known etiology for a particular form of autism, you can still see a lot of variation in the ultimate phenotype, right?

MR. PADGETT: Object to form. Go ahead.

THE WITNESS: What I can tell you is, you know, generally speaking, I can't answer that question, but with respect to specific genetic causes, I know that in two brothers, for example, with the exact same mutation can have a slightly different -- somewhat different presentation, yes.

BY MS. HUNT:

Q Okay. And is it fair to say that the science

around the etiology of autism is still evolving?

A All of science is always evolving and is still evolving, and I would say that there's little controversy over the fact that genetics are the -- the main majority known cause of both disorders to the tune of over 75 to 80 percent at the current -- is the current thinking.

Q Okay. Meaning that at least 20 to 25 percent of autism cases have environmental inputs?

MR. PADGETT: Object to form.

BY MS. HUNT:

Q In other words -- does that make sense?

A No.

MR. PADGETT: Same objection.

BY MS. HUNT:

Q Okay. So I think the statement you made is that 75 to 80 percent of the -- of the known causes of autism are genetic.

Does that mean the remainder are environmental?

MR. PADGETT: Object to form.

THE WITNESS: It does not.

BY MS. HUNT:

Q Okay. What's going on with the other 20 to 25 percent?

A Well, first of all, I would say that one of the foremost experts on genetics of autism, Dr. Wendy Chung,

feels that, you know, that is the number for inheritance and inheritability in twin studies, and what's not accounted for in those numbers, and the same is true, to some extent, for ADHD, are the rare de novo mutations that may account for on the order of 10 to 15 percent of ASD.

And I don't think we really have a good handle on what causes the rest of autism.

Q Are you aware that Dr. Chung published an article a couple months ago with Dr. Pearson?

A I haven't seen that paper, if that's what you're asking.

Q Okay. But are you aware that they co-published it?

A I think there was a reference to it in one of the depositions.

Q Do you know Dr. Chung personally?

A Not really, no.

Q Okay.

A I mean, she's famous, so I know of her.

Q Yes.

A I've spoken to her at meetings, briefly.

Q She's a big deal, I hear you.

Are you aware that the paper that she co-published with Dr. Pearson is actually about how environmental factors disproportionately impact genes related to

neurodevelopmental disorders?

MR. PADGETT: Object to form.

THE WITNESS: Well, I'm sorry.

Can you clarify what tissue we're talking about? Blood, brain, fetal brain, liver, kidney, skin.

BY MS. HUNT:

Q I'm happy to show you the paper if you'd like to take a look at it later. I'm just asking if you're aware of the subject matter of the paper?

A I have a vague conceptual understanding of what that paper might or might not be about, but again, I've never seen the paper, and the only reference I'm aware of in the -- that I've read in the literature about that is the reference that -- very cryptic and tangential references to that paper in, I think it was Dr. Pearson's deposition.

Q Okay. And you made some pretty serious accusations about Dr. Pearson in your expert report.

I think you said that his report raises concerns about the misuse of science; is that right?

MR. PADGETT: Object to form.

THE WITNESS: First of all, I did not make any ad hominem attacks that I'm aware of in my report.

I was talking about the things, ad hoc.

BY MS. HUNT:

Q Okay. We can come back to that later.

Okay. So going back to the question of the state of the science on autism in general.

Would you agree with me that we're not at the stage yet where we can do a blood draw and determine if an individual has autism?

A We are not at -- we cannot do that currently.

Q And same for ADHD, right?

A Yes.

Q Okay. And is that because we don't have specific biomarkers yet that can definitively tell us that a person has autism?

A I think that's a little broad. I would narrow that and say we have behavioral biomarkers to diagnose autism and ADHD, and we don't have a single test -- well, that's not true.

We don't have a blood test or a biopsy or an imaging finding that would diagnose someone with autism or ADHD, that I'm aware of.

Q Okay. And this may seem obvious, so just bear with me, but there's no way to look at what's going on in the fetal brain and then follow that child out six or seven years to see if they have ASD or ADHD, right?

A No. Incorrect.

Q You can look at what's going on in the fetal brain and then track that child out to six or seven years of age?

A Well, yes. You can see a fetal MRI and watch the growth trajectory over time of the fetal brain, and then look later to see if they have a diagnosis of autism spectrum disorder or ADHD.

Q Can you do a neurochemical analysis of what's going on in the baby's brain?

A I don't believe so, no.

Q Could you do a histology analysis of what's going on in the baby's brain?

A Not in a human.

Q Okay.

A Well, not in a human. In the way that you stated where you later can know whether they had autism or not, or ADHD.

Q And that's part of why the animal models can be helpful, right, because we can do that more invasive testing; is that fair?

A To look at potential mechanisms, I think that's a reasonable --

Q Okay.

A -- way to think about it.

I can tell you that if you find a mechanism in a rodent model, it may or may not be relevant to the human.

Q Okay. And when you're doing behavioral neuroscience work in animals, do you feel like it's

important to take into account how those conditions present in the real world in humans?

A That's an interesting question. That's very broad, but let me see if I can try to answer it.

In my experience --

MR. PADGETT: Object to form.

THE WITNESS: -- we study, for the most part, causes of autism, and we're trying to understand how that cause of autism changes brain function.

We may find hundreds of thousands of things wrong with the brain if we look at it hard enough. And then one of the endpoints we look at is rodent behavior.

In my view, every -- many people who aren't in the field look for changes that have face validity for autism spectrum disorder, for example. And we do too, and sometimes we find that and it lines up very well in terms of the loose face validity insofar as you can have any connection to a human being's behavior in a rodent.

In my work, if there's a behavioral difference, I look to see if the changes in the brain might correct that behavior, and that may or may not be relevant to a human.

BY MS. HUNT:

Q Is it important to understand, for example, the background rate of autism when you're designing these experiments?

MR. PADGETT: Object to form.

THE WITNESS: I'm not sure what you mean. The background rate of autism in rodents is zero.

MS. HUNT: No, I mean in humans, Dr. Powell.

MR. PADGETT: Same objection.

THE WITNESS: So, again, I don't -- could you explain it? I don't really understand.

MS. HUNT: Yeah. So I can rephrase the question.

BY MS. HUNT:

Q So when you're working with these mouse models, let's just use the Shank3 mice as an example.

Is it important for you to understand how the syndromic form of autism caused by Shank3 mutations presents in humans, or do you not care about the human context when you're working with the mice?

MR. PADGETT: Object to form.

THE WITNESS: Well, a two-part question.

I do care about the human context to some degree when I'm working with the mice, and I sort of lost the first part of your question.

BY MS. HUNT:

Q That's okay.

Do you -- do you ever look at epidemiological studies as part of your work in rodent models?

A Yes, I do.

Q Okay.

A And I have periodically looked at the literature of these epidemiology studies, and I always have -- since I started working on autism, since I opened my lab, every time I see an epidemiologist, I ask him, what's new, and, you know, is there something that I can hang my hat on that's causal that people aren't really working on.

You know, and then I would love to have a very clear cause that's environmental that I could study in the way that we do genes.

Q Mm-hmm. And the question of acetaminophen causing neurodevelopmental issues could be potentially resolved with a double blind randomized-controlled trial; is that fair, assuming that we're ethical?

MR. PADGETT: Object to form.

THE WITNESS: If you're speaking about randomizing pregnant women to receive doses of Tylenol without a clinical indication, I would say, no, that study would not be possible.

BY MS. HUNT:

Q Right. It wouldn't be ethical, right?

A I would agree with that.

Q Okay. But if it were -- if we didn't have to worry about the ethical considerations, would that give you a definitive answer about acetaminophen as a potential cause for neurodevelopmental disorders?

A It could if it was well done and reproducible by, independently, another group.

Q Okay. Because randomized control trials are most definitive evidence that you can typically get about a compound's effect on a human being, right?

A In a human being, yes.

Q Okay. And if we were able to do that study in humans, would you revisit your opinions in this case?

A At all times I am willing to revisit my opinion in this case based on peer-reviewed scientific literature.

Q Okay. Dr. Powell, do you describe yourself professionally as a neurobiologist?

A In part, yes.

Q Tell me about the other part.

A Well, I'm an M.D. neurologist. I practice in the hospital. I direct a center. I have some -- I direct a -- I'm a chair of a department.

I run an institutional behavioral core on -- for

rodents. I run my lab. And I direct now this year, starting in July 31st, a 10-week second year medical school course on all of neuroscience, including psychiatry and neurology.

Q Okay.

A And other things, but that's the gist.

Q Anything else?

A I reserve the right to say something else, but I think that sums it up in a broad stroke.

Q Okay. Do you consider yourself to be a toxicologist?

A I do not have a Ph.D. in toxicology, per se, although I have done studies that are relevant to toxicology. I've published in the toxicology journal and reviewed papers for a toxicology journal in the past.

Q Are you a member of any professional organizations for toxicologists?

A I am not.

Q Okay. And you're aware that people who specialize in toxicology or neurotoxicology undergo specialized training, right?

A I would say they do. Not every -- well, wait a minute.

Could you rephrase the question, or repeat the question? I might have missed something there.

Q Sure.

Are you aware that people who specialize in neurotoxicology undergo specialized training related to that discipline?

A I'm aware that some people do toxicology experiments without a Ph.D. in toxicology, and I'm aware that toxicology Ph.D.s undergo special training for toxicology research, yes.

Q Is it your understanding that you have to have a toxicology Ph.D. in order to perform a toxicology experiment?

A No.

Q Okay.

A Many people have a master's of public health perform epidemiologic studies which is relevant to toxicology and there are other examples.

Q Have you ever done any specialized training in neurotoxicology?

A Specialized training in neurotoxicology?

MR. PADGETT: Object to form.

THE WITNESS: If you mean a core or sort of post-doctoral fellowship or Ph.D.? No.

If you mean learning about it in the literature which I was trained to do, yes.

BY MS. HUNT:

Q Okay. So is it fair to say that your experience in neurotoxicology is learning about it by reading papers?

A Papers, books --

MR. PADGETT: Object to form.

THE WITNESS: Papers, books, conversations with toxicologists, epidemiologists, public health professionals, and reading the literature and attending autism and neuroscience meetings, among other things.

BY MS. HUNT:

Q Have you ever done a study evaluating the impact of a compound on the developing brain?

A Not on the developing brain, no.

Q Okay. Have you ever published on ADHD?

A I would say that I've published on genetic animal models that have hyperactivity and tried to relate them to a neurodevelopmental disorder.

Q Was that neurodevelopmental disorder ADHD?

A In part, yes, but not the only one.

Q Okay. Which study was that? If we can take a look at your CV.

A There's a study titled -- oh, gosh.

Q You know what --

A It has schizophrenia in the title, and it's about RIM1 --

Q Oh, I'm familiar with that one.

A -- alpha. The mice are hyperactive, and I gave them drugs that would treat ADHD with the idea that if it decreased their activity, then that might be some predictive validity for treatments for ADHD. It did not.

It actually gave them -- they actually had a bigger response to amphetamines and MK-801, which are psychoneurotics and enhance the potential connection with some face validity to schizophrenia.

Q So was that study about animal models of schizophrenia or animal models of ADHD?

A The study was about a genetic mutant that had hyperactivity.

Q Okay.

A And I studied it with the idea of seeing whether it might be relevant to ADHD or other neuropsychiatric disorders.

Q Okay. Other than that study, have you published anything else on ADHD?

A Not that I recall, no.

Q Okay. And outside of litigation, other than that one study, have you ever worked on or interpreted mouse models of ADHD?

MR. PADGETT: Object to form.

THE WITNESS: I don't believe that I've

personally worked on one of the touted animal models of ADHD, no.

BY MS. HUNT:

Q Okay. I would like to go back to your report for a second. Still in the first page.

You say in paragraph 2 that you were asked to perform a systematic review of all the published animal studies reporting neurodevelopmental outcomes following prenatal administration of acetaminophen to determine whether these data provide sufficient scientific evidence of a biological mechanism by which maternal use of acetaminophen during pregnancy might cause neurodevelopmental disorders in children.

Did I read that reasonably correct?

A You read that sentence in an introductory paragraph correctly. If you want more specifics, you should look at paragraph 4.

Q Don't worry, Doctor. We'll -- we will get there.

A I'm not worried. Thank you.

Q So was it your decision to do a systematic review or is that what you were asked to do?

A I was asked.

MR. PADGETT: I'll object to form.

THE WITNESS: Are you -- I just want to make sure. You're asking me what the attorneys in this case

for the defendant asked me to do?

BY MS. HUNT:

Q No. I'm not asking you anything about what the attorneys asked you to do.

I'm wondering if it was your decision to perform a systematic review rather than a weight of evidence analysis?

A Oh, I see what you're saying.

It was my decision to review the literature with respect to the quality of the evidence and the character of the evidence and the potential relevance to these questions of causality and biologically plausible mechanisms, if there are any.

Q So why did you frame it as a systematic review rather than a weight of evidence analysis?

A Because they're essentially, in my mind, very similar. I mean --

Q Okay.

A -- you systematically go -- in a weight of the evidence review, my understanding is you systematically go through the evidence and you look for any potential flaws, or, you know, how they did the science, and you make comments on that and come to your opinion.

Q I'd like to show you another exhibit, Dr. Powell.

So what I'm hearing you say is you don't have a problem with a weight of evidence approach; is that fair?

MR. PADGETT: Object to form.

THE WITNESS: Generally speaking, I have some issues with some applications of the weight of the evidence approach.

BY MS. HUNT:

Q That's fair. But reasonable scientists can disagree, right? I'm talking about, do you have an issue with the methodology itself?

MR. PADGETT: Object to form.

THE WITNESS: I would say that that's a very general question, I'll try to answer as best I can.

I think that the weight of the evidence and/or a systematic review is a reasonable way to analyze the body of literature, and if it's applied consistently and in a reproducible manner, I think that it's a reasonable way to go.

BY MS. HUNT:

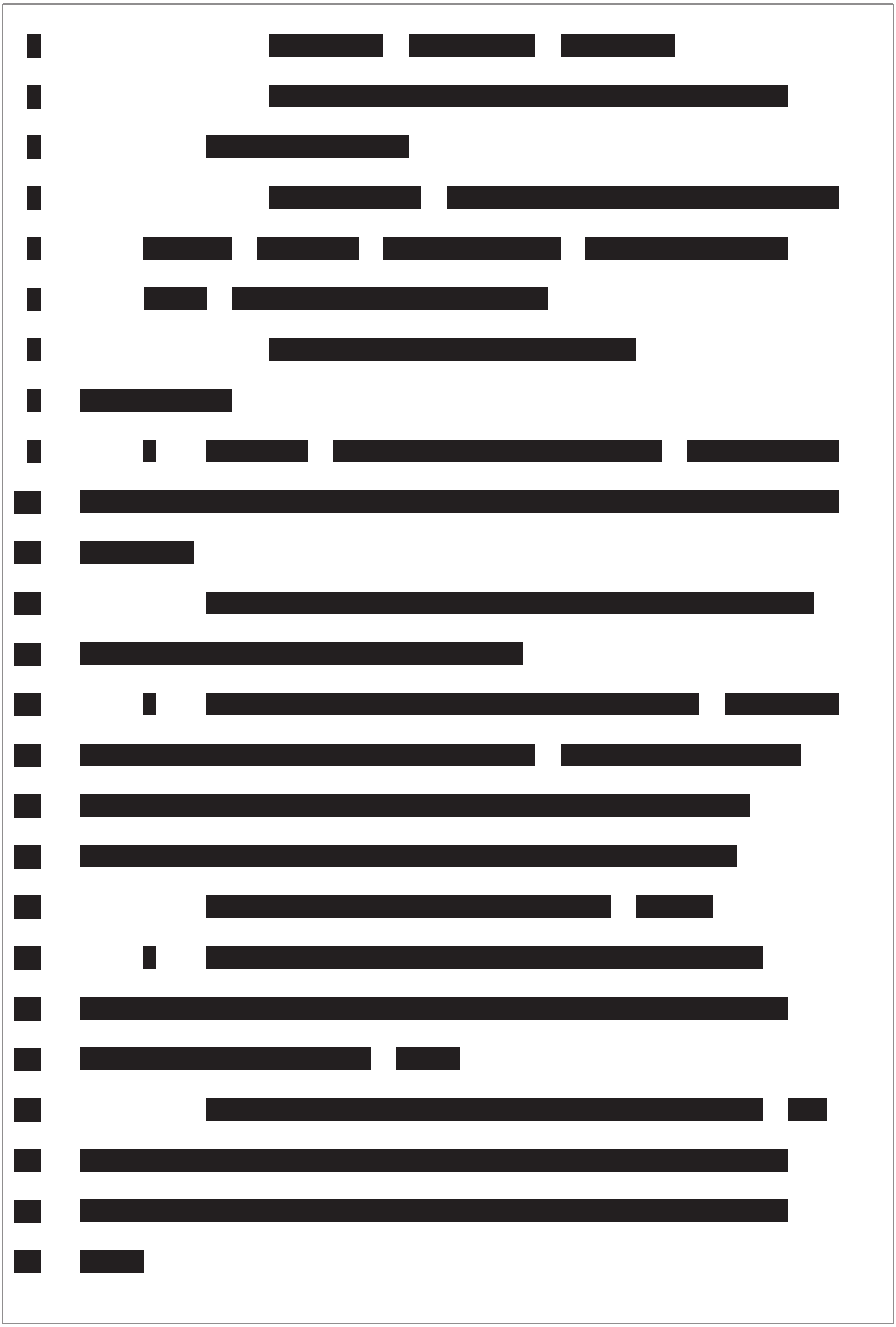
Q Okay. All right. So I'd like to take a look at this exhibit together.

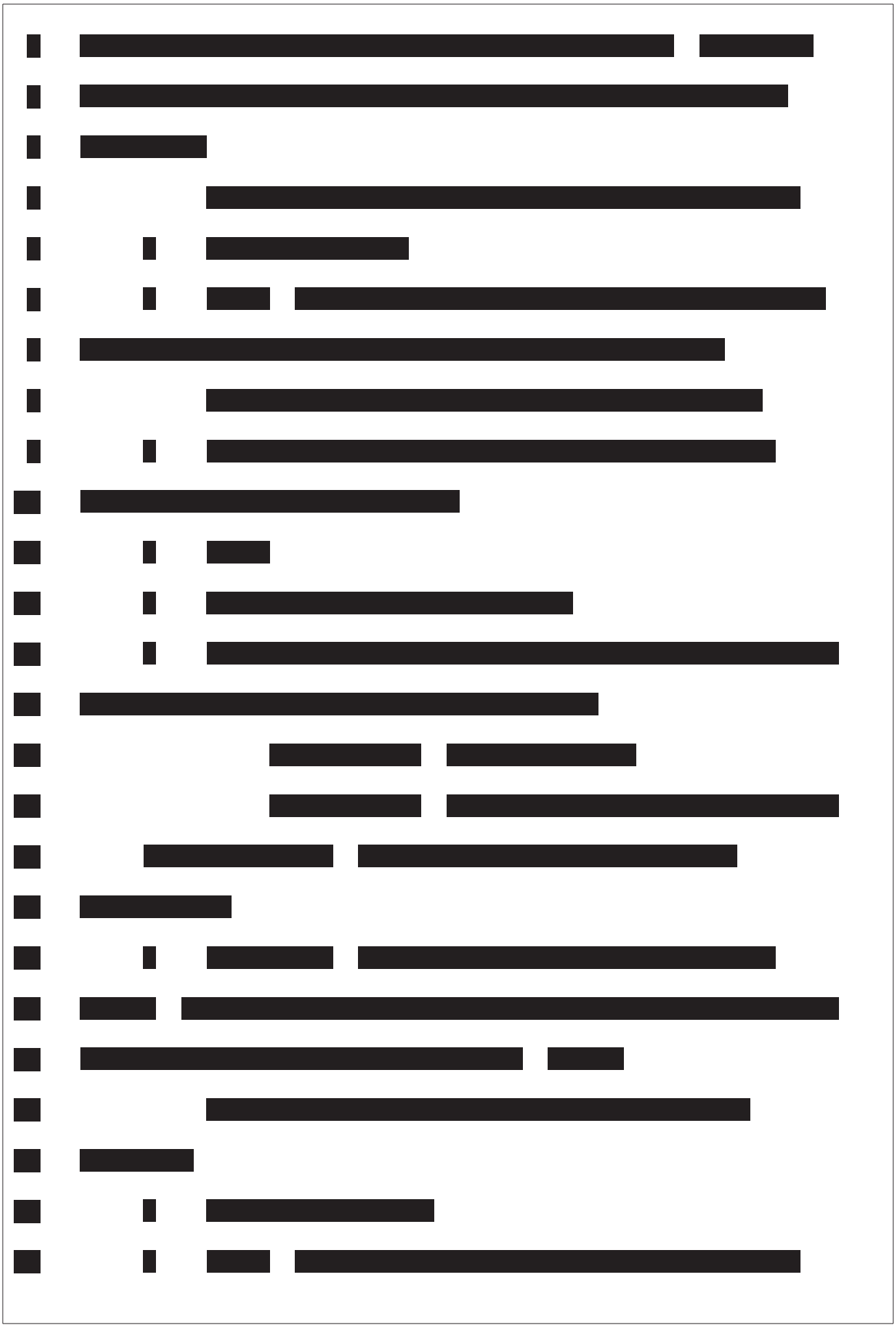
And if you see the first page, I think you'll see a Johnson & Johnson Consumer, Inc., logo in the top right corner, and then it says: "Our Approach."

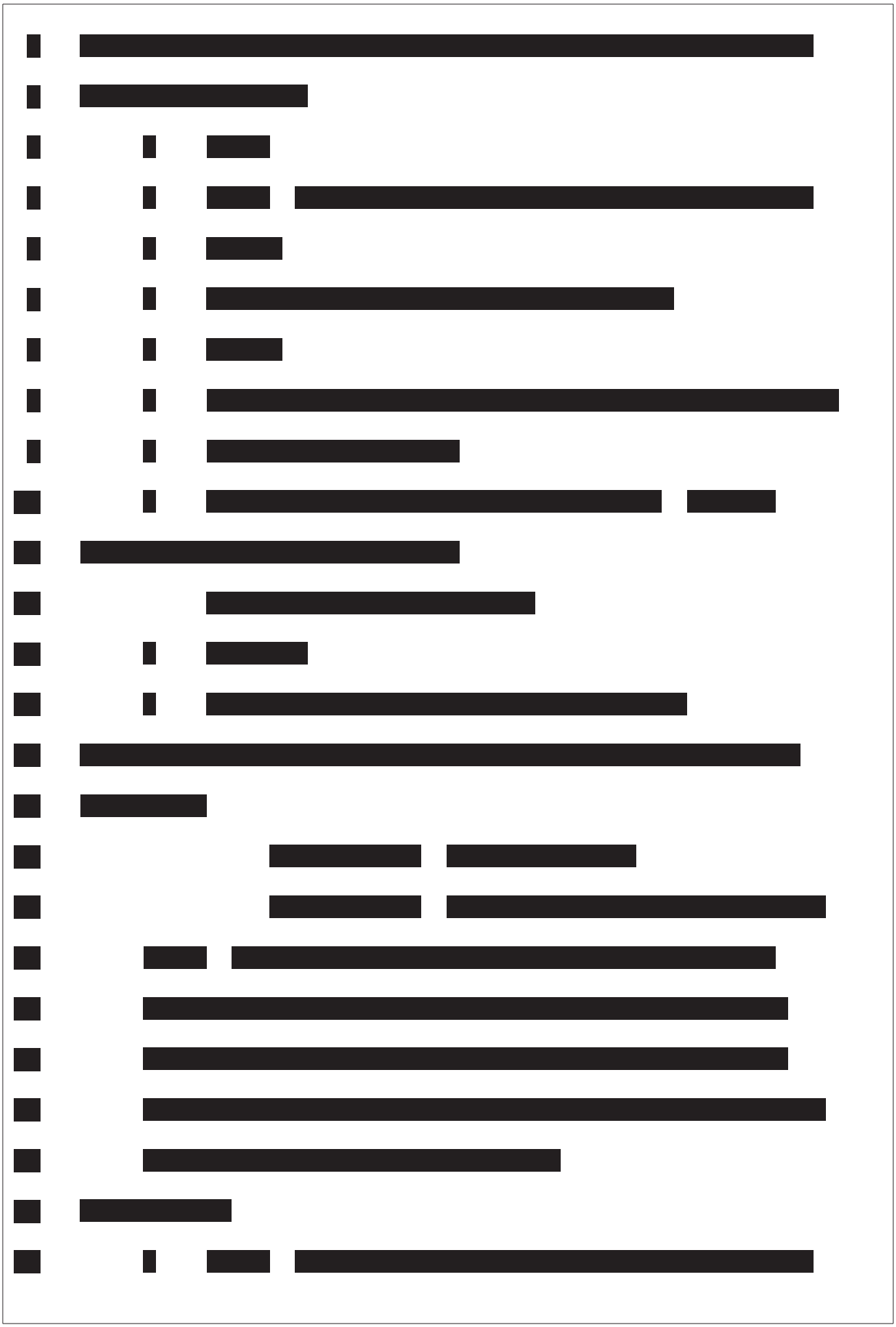
Is that right?

A That's what it says, yes, ma'am.

MR. PADGETT: Do you have a number?







If we go to page 44 of your report, which is marked as Exhibit 201.

In subsection H -- so, first of all, I should say this heading says: "Some of the studies I reviewed cannot inform the question at hand for various reasons. Such reasons include the following."

And then if we go down to H, it says: "Cultured cells not living organisms."

So, Dr. Powell, my question is: Did you take, for example, in vitro or ex utero data into account in your systematic review?

A I did. What I will say is in my initial analysis of the literature, I focused largely on in vivo studies, which I believe to be the most relevant.

And I did look at the culture studies and most of the culture studies that I looked at used what most of the experts in this case that opined on it on both sides would consider higher than the typical concentration in humans.

Q Okay. But, Dr. Powell, your report, if I'm just reading what's black and white on the page here, it says: "Some of the studies I reviewed cannot inform the question at hand." And those reasons include that they were in cultured cells, not living organisms.

So I guess I'm still stuck on the same question, and that's: Did you deem ex utero and in vitro studies as

irrelevant in your systematic review?

A Insofar as I was asking the question in my initial review, if the in vivo rodent studies provided evidence of causality in humans for ASD and ADHD, or biologically plausible mechanisms whereby that might -- if that outcome happens, that might occur. I deem them irrelevant to that initial question.

Later in my report, you'll see that I commented on the -- the cultured cells, among other studies.

Q Okay. So how is somebody reading your report supposed to know whether you considered them or didn't consider them?

A They would read my report and they would see the section where I considered them.

If you would log me in real quick? I don't remember the -- I mean, I thought I remembered.

MR. PADGETT: Just for the record, he -- there's an electronic version of his amended report on here and he has access to nothing else.

MS. HUNT: Why don't we do that on a break, and I can come back to this.

And actually, we're at about an hour, if this is a good breaking point.

THE WITNESS: I'm fine. Whatever you want to do.

MS. HUNT: If he needs time to look, I'd rather just do it off the record and take a break since we're an hour in.

THE VIDEOGRAPHER: Off record. 9:27 a.m.

(Off the record at 9:27 a.m.)

THE VIDEOGRAPHER: On record, 9:42 a.m.

BY MS. HUNT:

Q All right. Dr. Powell, I would like to see where we can find some agreement, perhaps, on the way acetaminophen affects the body.

So, first, do you dispute that acetaminophen can form NAPQI in the body?

A And by -- when you say "body," do you mean to include the nervous system, including the central nervous system or not?

Q Okay. So how about we start with the whole body.

Can it form NAPQI in the body in general anywhere?

MR. PADGETT: Object to form.

THE WITNESS: I believe that it can. That's part of the known metabolic -- metabolism of acetaminophen in the liver.

BY MS. HUNT:

Q Okay. Do you believe that NAPQI can form anywhere besides the liver?

A That's an interesting question. I'm not sure I

know the answer to that.

Q Okay.

A Based on the information that I reviewed.

Q Okay. And NAPQI is formed through CYP2E1 enzymes, right?

A My understanding is that that is the, in large part, that's the major enzyme that does that, yes.

Q Okay. So if a tissue or an area in the body has acetaminophen and it has CYP2E1, would your assumption be that NAPQI can form there?

MR. PADGETT: Object to form.

THE WITNESS: No.

BY MS. HUNT:

Q Explain why not.

A Well, it depends on what you mean by "there," right?

So it would depend on how much was there, what other metabolic pathways were active. And I would need to see data that suggests that, you know, like in the liver, that there's multiple pathways for detoxifying or de -- I'm sorry, metabolizing in rendering safe acetaminophen in whatever organ you're referring to.

Q Okay. So are you aware that NAPQI can form in the kidneys?

A I didn't -- I don't have -- I didn't review that

information for this, my report or this deposition, so I'm not aware.

Q Okay. Are you aware that NAPQI can form in the lungs?

A I didn't study the lungs, CYPE enzyme or NAPQI formation in the lungs.

Q Okay. Do you know if NAPQI can form in the brain?

A I don't recall seeing any literature measuring NAPQI formation in the brain.

Q Okay. But it's hard, if not impossible, to measure NAPQI, right?

A Well, it's incredibly short lived, isn't it, yes.

Q And so isn't one of the ways that scientists determine whether NAPQI was there, examining oxidative stress?

A I would say examining oxidative stress is a way that scientists would look to see if there had been any oxidating -- oxidating -- any oxidation going on in the brain.

Q Okay. And is it your understanding that NAPQI causes oxidative stress?

MR. PADGETT: Object to form.

THE WITNESS: Sorry. It's my understanding that NAPQI is an oxidizer.

BY MS. HUNT:

Q Okay. There's a part of your expert report which we've marked as Exhibit 201, it's on page 83, and it is in the middle of paragraph 184.

You say that "glutathione is the antioxidant supposedly depleted by acetaminophen exposure."

And I know that's in the context of a longer sentence, but do you dispute that NAPQI can deplete glutathione?

MR. PADGETT: Object to form.

THE WITNESS: In high doses, NAPQI may be able to deplete glutathione. I'm not aware of any evidence that suggests that GSH is depleted, as I understand the word, by typical doses of acetaminophen in the liver, or anywhere else in the body.

BY MS. HUNT:

Q Are the levels of glutathione in the body affected by acetaminophen intake?

A I believe that's been demonstrated, yes, in the liver for sure.

Q How about in other organ systems in the body?

A I think I read some literature regarding decreases in the adult brain of GSH on the order of about 10 percent or so.

Q Okay.

A If I'm remembering correctly.

Q And do you agree with me that oxidative stress can be dangerous to the developing brain?

MR. PADGETT: Object to form.

THE WITNESS: Again, it depends on what you mean by oxidative stress.

To explain, I would say that insofar -- if there were oxidizing agents in the brain that were not reduced by GSH, they could potentially oxidize things in the brain.

BY MS. HUNT:

Q And if there were not enough GSH to act as an effective antioxidant in the brain, that could be a problem, right?

MR. PADGETT: Object to form.

THE WITNESS: Well, first of all, I've seen no evidence that that's the case and --

BY MS. HUNT:

Q I'm not talking about acetaminophen, let me be clear. I'm sorry to interrupt you.

I'm saying in general, if there is not enough glutathione in the brain to act as an effective antioxidant, could that be a problem for neurodevelopment?

MR. PADGETT: Object to form.

THE WITNESS: It's possible.

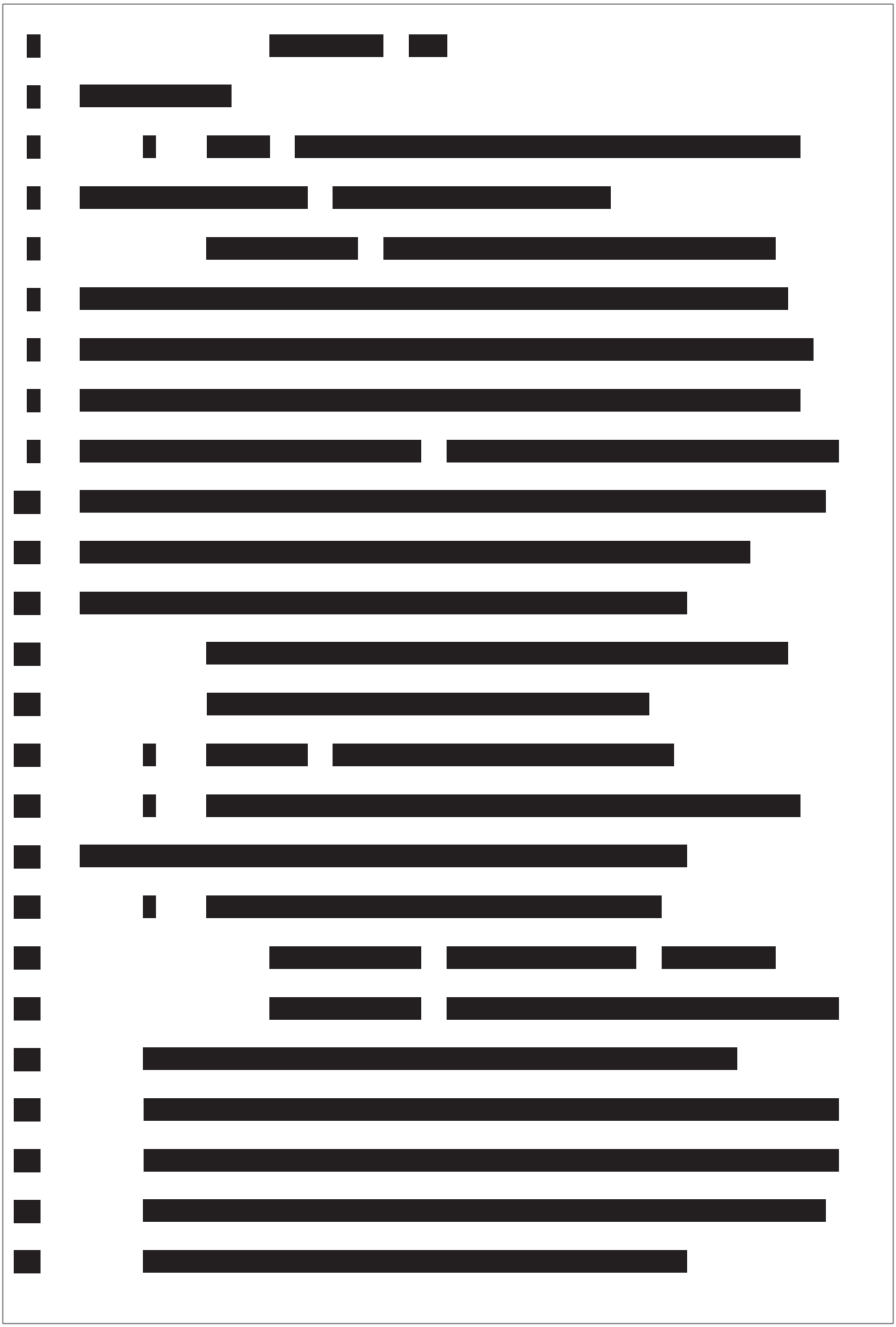
BY MS. HUNT:

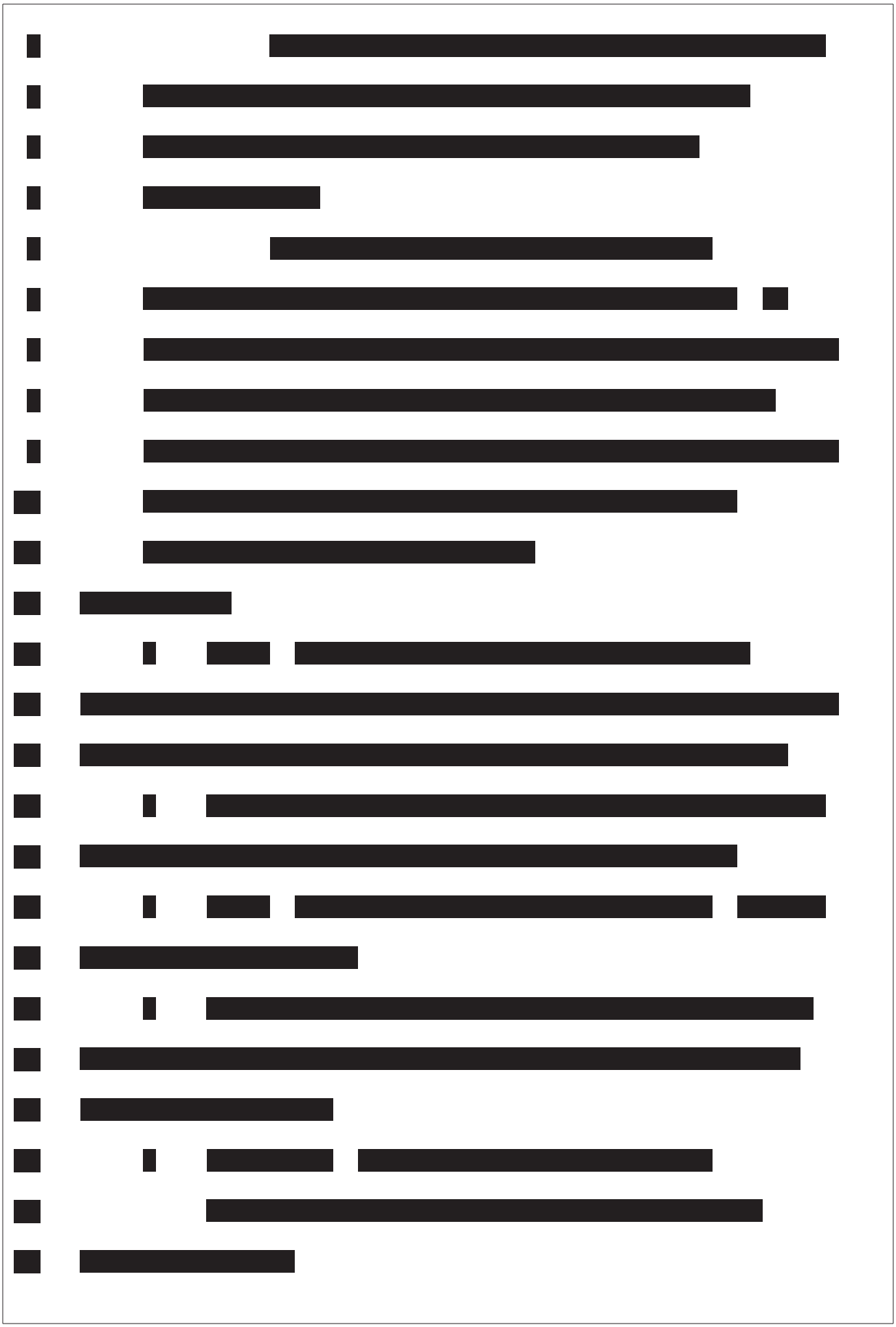
Q Okay. Do you agree with me that acetaminophen can interact with the endocannabinoid system?

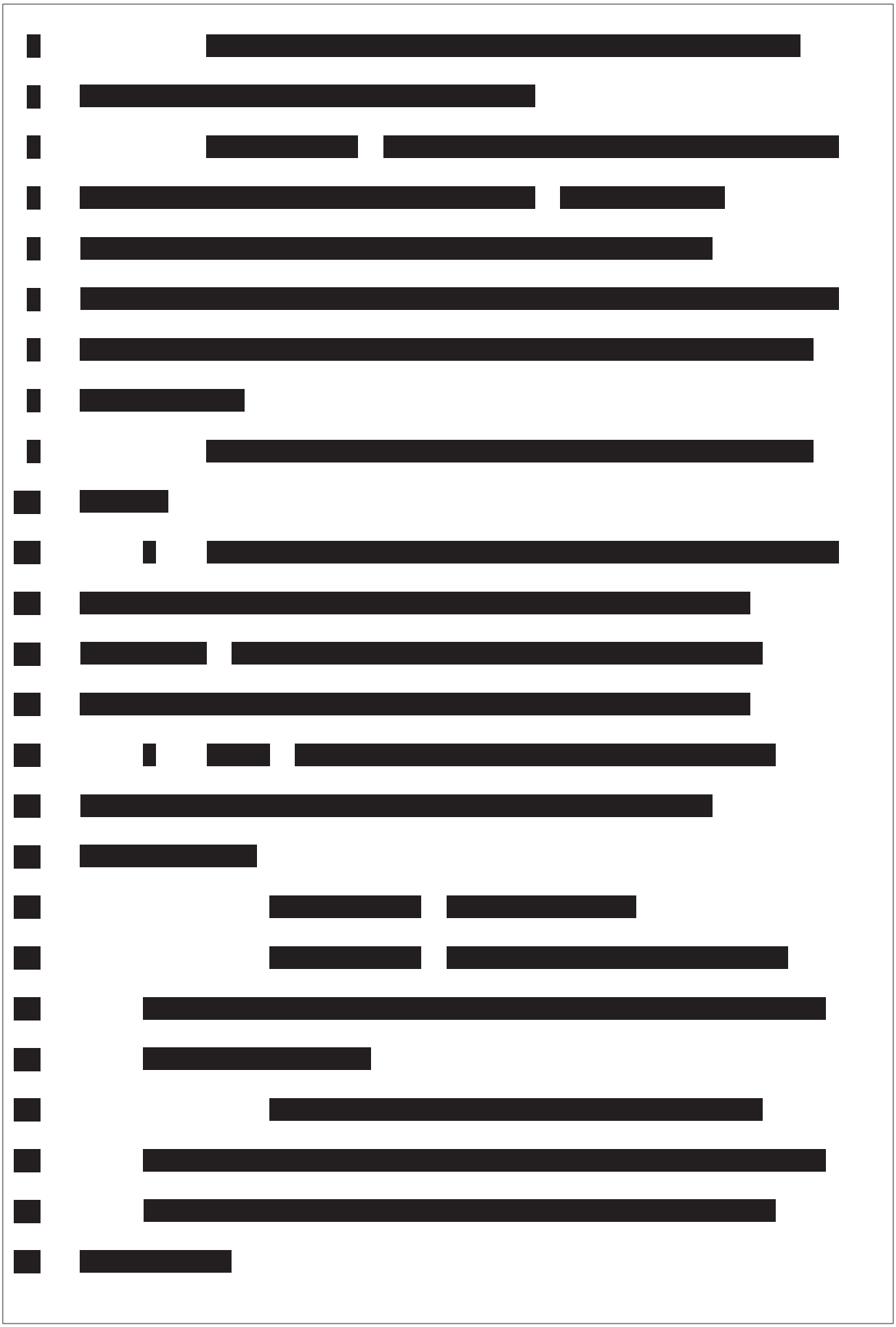
MR. PADGETT: Object to form.

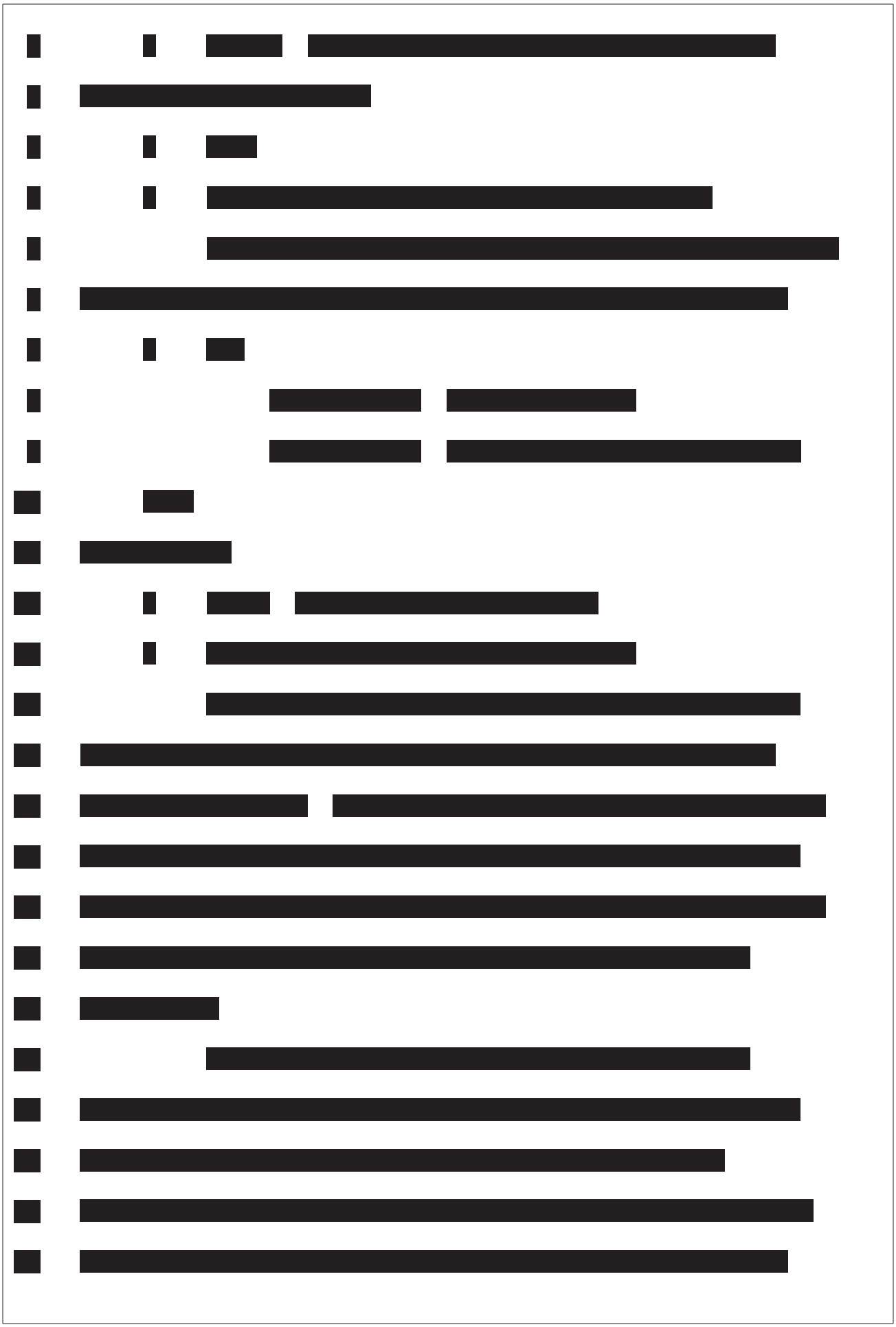
THE WITNESS: I know of no data that suggests that acetaminophen in vivo has increased levels of anandamide or AM404 in the literature that I've reviewed.

BY MS. HUNT:









[redacted]

Did you list that on your Materials Considered List anywhere?

MR. PADGETT: Object to form.

THE WITNESS: I don't believe I put that specific paper, no.

BY MS. HUNT:

Q Did you take it into account when forming your opinion in this case?

A What I would say is, I was -- I looked for evidence that acetaminophen acted on endocannabinoid pathways, and I read data that showed that there was -- that blocking or antagonizing CB1 receptors was postulated as a potential possible mechanism of acetaminophen's analgesic actions, and I've explained to you the two possible interpretations of those data, and I considered that literature in forming my opinions in this case, to some degree, but -- and I don't remember whether I've cited any of those studies or not.

Again, I believe in my report I have mentioned AM404 as a possibility in various places, and, again, stated whether or not there was literature that it forms in the brain, I think maybe, but I'm not 100 percent sure.

Q Okay.

A Acetaminophen -- okay. I did address this on paragraph 98 in reference to the Bauer, et al., summary review of the sum of the literature on acetaminophen.

Q Okay. And, Doctor --

A And it suggested that acetaminophen might act through the endocannabinoid system.

Acetaminophen inhibits cyclooxygenase enzymes that degrade endocannabinoids. Meaning that acetaminophen would be predicted to increase endocannabinoids in their actions along with conjugation into AM404.

It's clear that any role for altered endocannabinoids in ASD remains understudied and uncertain. And I have a reference there.

If anything --

Q Doctor, I'm sorry. I'm going to have to stop you. I asked if you had considered this specific article.

A And, ma'am, I'm going to interrupt you, and I'm sorry, but I am explaining to you exactly where and how I considered it as an answer to your question. I'll continue.

If anything, cannabinoids are reduced in patients with ASD and cannabinoids may actually alleviate some of the symptoms associated with ASD.

And I go on.

Q Okay. And do you cite Hogestatt anywhere in that

long section?

MR. PADGETT: Object to form.

THE WITNESS: In paragraph 98, I do not.

MS. HUNT: Okay.

THE WITNESS: And I do not have Hogestatt as a reference. And as I told you, I read other papers that had similar findings.

MS. HUNT: Thank you for answering my question, Doctor.

BY MS. HUNT:

Q Do you agree with me that endocrine disruptions can be dangerous to the developing brain?

MR. PADGETT: Object to form.

THE WITNESS: I'm not sure I can answer that question because, you know, dangerous is -- can be a relative term.

BY MS. HUNT:

Q Okay. So sitting here today, you can't tell me if endocrine disruptions during neurodevelopment are a good or bad thing?

MR. PADGETT: Object to form.

THE WITNESS: What I can tell you is: I'm not aware of any data that endocrine disruption contributes to autism spectrum disorders or ADHD, which is what I reviewed and certainly not in the rodent

literature, that I understand that there are some studies looking at potential reproductive effects of acetaminophen on endocrine pathways.

And I also have stated in my report that the types of endocrine disruptions would actually be, you know, based on a conceptual understanding. They might be lowering testosterone, for example, perhaps, and that would tend to -- if you look at the -- I think I stated in my report that if you think about the extreme male brain hypothesis of autism, or theory of autism, if you will, having decreased testosterone would potentially be protected, but that's all I have to say about that.

BY MS. HUNT:

Q Could a reasonable scientist believe that endocrine disruptions during pregnancy are dangerous to the developing brain?

MR. PADGETT: Object to form.

THE WITNESS: I would say a reasonable scientist could believe a lot of things.

I believe a reasonable scientist could be aware that some neuroendocrine effects on the brain may affect the body in terms of development of genitalia, for example.

BY MS. HUNT:

Q Okay. I think I asked specifically about the brain, so I'm going to ask that question again.

Could a reasonable scientist believe that endocrine disruption during pregnancy is dangerous to the developing brain?

MR. PADGETT: Same objection.

THE WITNESS: It's just too broad of a question. I don't know what you mean by "dangerous."

I don't know what --

MS. HUNT: Harmful.

THE WITNESS: -- you mean by -- hurtful in what way?

MS. HUNT: Perturbing neurodevelopment.

THE WITNESS: Perturbing neurodevelopment.

MR. PADGETT: Object to form.

THE DEFENDANT: It's possible that endocrine disrupters may affect some of the hormonal system -- regulation systems in, say, the hypothalamus that might lead to subtle or not -- or depending on the dose, not so subtle changes in genitalia, among other things, is a possibility, yes.

BY MS. HUNT:

Q Are you aware that ACOG and other organizations encourage women to avoid endocrine disrupting substances

during pregnancy?

MR. PADGETT: Object to form.

THE WITNESS: That's not a topic that I've looked at in depth. I'm aware that they -- what are you talking about, the ACOG?

MS. HUNT: That's okay. We can move on.

BY MS. HUNT:

Q Is it your understanding that acetaminophen can affect serotonergic signaling in the brain?

A I would say that it's possible, and I have not -- I don't recall seeing specific data that's consistent and reputable, that's relevant to the question under consideration in my report, that suggest that that supports that possibility in the brain of a fetus.

Q Okay. So, again, I'm going to repeat my question because I'm afraid we're talking past each other here.

What I'm asking is: Is it your understanding that acetaminophen can affect serotonergic signaling in the brain?

MR. PADGETT: Object to form.

THE WITNESS: It's my understanding that it's a possibility. And it's my understanding that -- I haven't seen the literature that's consistent and reputable that suggests that there's an alteration of serotonin signaling in the fetal brain with

acetaminophen at doses recommended equivalent -- doses that we would consider equivalent to human recommended doses.

BY MS. HUNT:

Q Okay. Can disruptions to neurotransmitters like serotonin be harmful to the developing brain?

MR. PADGETT: Object to form.

THE WITNESS: If they're dramatic and severe, it's possible, yes.

BY MS. HUNT:

Q Okay. And would you agree with me that it's not just genes, but gene expression that is important for neurodevelopment?

MR. PADGETT: Object to form.

THE WITNESS: Gene expression patterns are happening in all -- changes in gene expression are happening daily, every moment -- virtually every moment of our existence in our brains.

When we learn something new, gene expression changes. Certain gene expression changes with circadian rhythm, the time of day, can change expression in the brain.

So I think gene expression is a fundamental process that can change in the brain and the body, period.

BY MS. HUNT:

Q Okay. And can changes in gene expression sometimes result in pathologies?

MR. PADGETT: Object to form.

THE WITNESS: Absolutely, yes.

BY MS. HUNT:

Q Okay. Do you agree with me that, in general, when you're evaluating a set of data, it's important to understand your initial hypothesis in science?

MR. PADGETT: Object to form.

THE WITNESS: It's important to understand -- well, there's two kinds of science; discovery science and hypothesis-driven science.

So it's not a requirement to have a hypothesis, but, generally speaking, we generate and formulate a hypothesis when we do research.

BY MS. HUNT:

Q And for purposes of forming your opinion in this case, did you start with a null hypothesis?

A I started with the hypothesis that -- well, actually, no.

I mean, I -- I -- the -- the question at hand was whether or not acetaminophen, during the human equivalent of gestation in rodents, has supported or provides any support for causality or a plausible biological mechanism whereby

acetaminophen may or may not.

The null hypothesis in that case would be that it does not cause -- that the acetaminophen does not cause autism spectrum disorder or ADHD, and that there would not be a plausible biological mechanism, so that would be the null hypothesis.

But again, when I did my report, I'm doing a systematic review, not an experiment, just to be clear.

Q So is it your opinion that it's not important to form a research question or a hypothesis before starting a systematic review? Or I'm sorry, a systematic review?

MR. PADGETT: Object to form.

THE WITNESS: That's not what I said. And that's not my opinion.

BY MS. HUNT:

Q Okay. Do you think that it's important to have a hypothesis of some kind when you're undertaking a systematic review?

A I think it's important to define the question at hand that you're addressing, which again, I told you what the question was, and I've told you what the null hypothesis would be.

Q But --

A Based on that question.

Q But did you begin with a null hypothesis?

A I began --

MR. PADGETT: Object to form.

THE WITNESS: Sorry.

I began with a question, and then the question implies what the null hypothesis is, and I've stated it.

BY MS. HUNT:

Q So is that a yes, you did begin with a null hypothesis? I promise you, I'm not --

A Actually, I began with a question, which implies the obvious, in my opinion, null hypothesis.

Q Okay.

A And I don't recall -- never mind.

Q Can you point to me where in your expert report, which again, we've marked as 201, where you say that you started with a null hypothesis?

MR. PADGETT: Object to form.

THE WITNESS: I can point you to paragraph 4, where it defines the question, but not a null hypothesis.

MS. HUNT: Okay.

THE WITNESS: I'm not aware of anybody who stated a null hypothesis before they did that bear systematic review by any of the expert witnesses in the case, but my memory may not be serving me at the

moment.

BY MS. HUNT:

Q And if you're starting with a null hypothesis and if there's no relationship between acetaminophen and these neurodevelopmental outcomes, you'd expect to see no effects across the studies, right?

MR. PADGETT: Object to form.

THE WITNESS: No. I think that's incorrect.

I would explain further by saying that, number one, the question regards a uniquely human disorder that cannot be diagnosed in rodents.

And it also -- my reading of the epidemiologic literature suggests that there's no evidence that acetaminophen causes ASD or ADHD in humans.

And I don't -- it's my opinion that when you start with a noncausal manipulation in a rodent model, that it lends any credence to causality for a human disorder, such as autism spectrum disorder or ADHD.

BY MS. HUNT:

Q So did you start with the assumption that administering acetaminophen was a noncausal manipulation in a rodent model?

A No.

Q Okay.

A I'm sorry. If you're speaking of -- well, I'm sorry.

If you're speaking of noncausal in a rodent model for the cause of a human disease that's defined by uniquely human behavioral changes, then I would say that I didn't -- that's not the case.

But if you're asking me if it causes effects in mice, I did not start with the hypothesis that -- or assume that it didn't cause effects in mice.

Q Okay.

A I looked at the literature to see what effects it did cause, how consistent they were, what the potential concerns are with each of the experimental approaches, consistency, and many other factors listed in my report.

Q And separate and apart from the question of whether it causes ultimate neurodevelopmental disorders as endpoints, did you see that acetaminophen caused changes in rodents in some of these studies?

MR. PADGETT: Object to form.

THE WITNESS: That's pretty broad.

I think my report makes it clear that the data on changes in substances or -- of inside the brain of the fetus, of rodents after acetaminophen administration, there were few -- few or -- there were -- I don't recall, as I sit here today, a

replicated finding of a change in molecular signals in the brain.

And if you're like any scientist, I looked for reproducibility and replication of behavioral findings, and I've noted, for the most part, that these behavioral findings are inconsistent across studies.

MS. HUNT: Okay.

THE WITNESS: Or unreplicated, or both.

BY MS. HUNT:

Q Okay. Are you done?

A I am.

Q Okay. All right.

I'd like to turn back to your report which, again, we've marked as Exhibit 201, and I'd like to look at page 33.

And I want to -- I want to understand your methodology a little bit better.

First off, are there any guidance documents that you used to inform your systematic review?

A Yes.

Q Okay. Can you tell me what those are?

A First of all, what I did was I made my own list of criteria that I would use. Then I looked in the literature at, for example, Gurusamy, et al., which is -- it was reference 36, I'm not sure what it is now.

I also looked at the Silverman paper on translation of autism animal models, the review that's cited by myself and some of your experts.

And I also looked at multiple iterations of the ARRIVE 2.0 guidelines, and all those things lined up pretty well.

Q Okay.

A So that resulted in the list of the criteria that's in my report.

Q Have you ever published another systematic review?

A I've published summative reviews, but not systematic reviews.

Q Okay.

A But I have systematically reviewed the literature many times in my daily research career.

Q But I'm talking about a formal published document. You've never done that previously?

A I've never published such a document, no.

Q Okay. And is the goal of a systematic review to be objective?

MR. PADGETT: Object to form.

THE WITNESS: The goal of a systematic review, in my understanding, is to shed light on the question at hand in an objective manner.

BY MS. HUNT:

Q Okay. And why is that objectivity important?

MR. PADGETT: Object to form.

THE WITNESS: Because what I would say is, objectivity's important because oftentimes review articles, I think summative reviews especially, can have an agenda pre-existing before they write it and that is not the case for my report, or my analysis in this case.

BY MS. HUNT:

Q Okay. And it would be -- it would be unscientific, right, to publish a review that had a preconceived conclusion; is that right?

MR. PADGETT: I'll object to form.

THE WITNESS: Did you say "systematic review"?

BY MS. HUNT:

Q I would say any kind of review article.

A I would say review articles are written all the time to try to support a particular person's or scientist's favored hypothesis. I think that happens quite a bit in the literature, even the peer-reviewed literature.

Q How about a systematic review, is it important to be objective and not have a specific endpoint in mind when you start?

A I think I've answered that.
Q Okay. How about in a weight of evidence analysis?
A Same.
Q Okay. How about in a review article about epidemiology?
A You're asking me if it's important to be objective in a review article about epidemiology, that's a summative review and not a systematic or weight of evidence review, correct?
Q Yeah. Well, I think in epidemiology they use a weight of evidence methodology called Bradford Hill, right?
MR. PADGETT: Object to form.
THE WITNESS: I'm aware of multiple reviews that don't use those criteria in the field of epidemiology. Bauer, et al., is one of them.
BY MS. HUNT:
Q Okay. But do you agree that, in general, when you're reviewing -- excuse me, a body of literature, it's good to be objective?
A It's always good to be objective, in my opinion.
Q Okay. And it's good to be transparent, right?
A I would agree with that.
Q And it's good to be transparent so someone can go behind you and reproduce your analysis if they need to, right?

A Well, insofar that there is an analysis done, I think that would be important, yes.

Q Okay. Okay. So going back to the spot I talked about in your report.

You say shortly before this that two studies passed all of your criteria, and you decided those two are relevant, and I believe those two are Saad and Baker 2023, right?

A So, I want to make clear that there were two parts to my systematic review.

One, the first one that we're speaking of was looking at the articles, and I've enumerated all the considerations and how those studies fall into different categories of that consideration.

And then if you look at paragraph 93, I ignored all the potential scientific flaws -- I think it's 93, or it's around 93. I ignored all the potential scientific flaws and took all the results at face value to determine, in a most conservative manner, what's left that replicates and that's believable.

Q Okay.

A There were two steps to my review.

Q Doctor, do you feel like you just answered my question?

A 100 percent.

MR. PADGETT: Object to form.

MS. HUNT: Court Reporter, can you read it back?

(Requested portion of the record was read back by the court reporter.)

THE WITNESS: Incorrect. What I -- what I actually did was I considered all the potential flaws, and if one looks at all those potential flaws and then looks at what's remaining after all those issues are -- papers with all those issues are set aside for the purposes of drawing the firmest possible conclusions, I told the reader what was left that met all of those criteria.

I never excluded any article in my analysis --

BY MS. HUNT:

Q Okay. So --

A -- for any reason.

Q Okay. So I think we're going to just need to take this one step at a time.

So let's go to page 29 of your expert report marked as Exhibit 201.

At the very bottom, there is a heading that says: "B. Results of Systematic Review."

Are you with me?

A I'm with you.

Q And then you say: "Of the 99 peer-reviewed original research publications evaluated in detail, only two publications passed criteria for relevance to the condition of concern and appropriateness of experimental design and statistical analysis."

Did I read that reasonably correct?

A You did.

Q Okay. And are those two studies Saad 2016 and Baker 2023?

A I'm just looking for the Saad paper. Yes, that is correct.

Q Okay.

A In that initial part of my analysis.

Q Okay. And then if we go to page 33.

You have a section at the top, it's subsection C. And it says: "Explanation of Critical Flaws in and/or Lack of Relevance of Remaining Publications Systematically Reviewed."

Did I read that reasonably correctly?

A Yes. You read it correctly.

Q And when you say "remaining publications," are you talking about all the papers besides Baker and Saad?

A When I talk about the remaining publications, explanation of critical flaws in and/or lack of relevance of remaining publications systematically reviewed.

Oh, yeah, that's a good point that you point out. Remaining may -- is probably the incorrect term that I would have used.

What I would say is this is the section where I outline which papers have which flaws --

Q Okay.

A -- in detail in reference to that initial portion of my analysis --

Q Okay. And --

A -- which we previously referenced.

Q Okay. And for someone to figure out why you found a study non-relevant or what flaws that study had, they need to look at the string of citations at the end of some of these sentences; is that fair?

A Among other things in the list format in subsequent pages, yes.

Q Okay. So, for example, if I turn to page 34 and I look at the subsection entitled: "Use of Excessive Drug Doses," right above paragraph 74.

Do you see that string of citations after the second sentence?

A I do.

Q Okay. And then if we turn to page 44 of your report, under the heading that says: "Non-Relevant Published Studies."

And we look at 91A, which says: "Findings confined largely to hepatotoxic, higher doses."

Do you see there's another string of citations there?

A I do.

Q Okay. I'd like to take a look at what we've marked as Exhibit 266.

(Powell Deposition Exhibit 266 marked for identification.)

BY MS. HUNT:

Q All right. And, Dr. Powell, we actually had to create this chart to try to understand which studies you excluded as non-relevant based on dose.

Were you aware, in writing this report, that you were only consistent about two studies in terms of their dose being overly high across these three sets of string cites?

MR. PADGETT: Object to the use of this counsel-created document, and its accuracy.

You can answer.

THE WITNESS: So --

MR. PADGETT: And to form.

THE WITNESS: -- in one of the previous paragraphs you cited, I clearly say that a dose in rodents above -- greater than 200 milligrams per

kilogram is -- it's -- first of all, it's a very conservative point.

So using allometric scaling, the dose in rats, max dose recommended for humans, corresponds to about 90 milligrams per kilogram. And so I've been overly conservative for rat studies by putting the cutoff at 200 milligrams per kilogram.

Similarly, for mice, I put it -- it would lead to an allometric scaling dose of around 150 milligrams per kilogram.

Again, my cutoff is higher.

And then as I went through these, I referenced studies that were confined to higher dose, spatic doses, higher than my cutoff, in two places.

And if you're saying that they don't line up perfectly, then that may be the case.

BY MS. HUNT:

Q Okay. I'm actually -- I'm saying they only line up in two places.

So I guess what I'm wondering is --

A Well, let's look at each of the places --

Q Yeah.

A -- so that we can better understand.

Q Yeah, I would be happy to.

A Sure.

Q So I think we already looked at 74 and 91A.
A 74. I don't think 74 speaks to dosing at all.
Oh, page 74 or paragraph 74?
Q Paragraph 74, Dr. Powell.
A My bad. I gotcha. Okay.
Q Okay. And then again --
A Paragraph 91A.
Q Yep. And that's page 44.
A So this is where I talk about non-relevant published studies that can't inform the question at hand for the following reasons.
And I've listed multiple citations.
Q Right. And I'm talking specifically about A, the --
A I understand.
Q Yeah.
A I see that.
Q About dose.
A Got it.
Q Okay. All right.
And then let's look at the third place, which is paragraph 116, and that's on page 55.
A I believe that's in the -- what page?
Q 55.
A 55. Thank you. In paragraph which?

Q Paragraph 116.

A Right. So --

Q I think it's the second sentence.

A Sure. I would say -- yeah, go ahead. What's your question? Sorry.

Q Well, and so I guess my question is: Is there a reason that you didn't just list in one place all the studies where you felt the dose was too high?

A Well, yes. For example, in 116, I only -- it was a rebuttal, I believe, to the -- I always get this wrong, plaintiffs' experts; Pearson, Cabrera, Louie, and maybe some of Hollander's, wherein they considered, in Pearson's case, approximately 24 or 25 in vivo rodent studies.

And Dr. Cabrera's, which brings the total to about 34 or so. And so I focused my rebuttal statements in paragraph 116 on those studies, and so that's the first explanation of why those might be different.

Q Okay.

A Secondly, what I would say is that in paragraph 74, I talked about studies that had high doses, and then there was a host of other studies referred to in paragraph 91A, which I consider sort of other reasons for excluding things.

And so I think that when I did paragraph 74, I was looking at a side of the literature, and in 91A, it's -- I

may have been thinking about things that hadn't already been excluded for other reasons or -- I didn't exclude any papers ultimately, but what I would say is the paragraph 91 was largely things that I -- that didn't exclude for other reasons, as best I can recall, but I agree with you that they aren't perfectly in alignment.

Q Okay. And would you agree with me that it might make it challenging for someone seeking to reproduce your systematic review to figure out which studies you had a dose problem with?

A No. Because I state exactly the criteria for having a problem with the dose.

Q Okay. And so --

A And so anybody could look at all those papers and replicate exactly what I've done.

Q So which list is it of these three? Is it -- is it all of them, is it paragraph 91A, paragraph 74, paragraph 116, or all three?

A Yes.

MR. PADGETT: Object to form.

THE WITNESS: It's all three.

I mean, the bottom line is that the goal that you're speaking of is to have someone be able to look at what I did and reproduce it.

That doesn't mean that they're going to

reproduce it by taking my word for it. They're going to do the systematic analysis exactly as I've done and they'll come up with their list of papers, and I believe it will overlap with these references.

Now, there may be a case in this initial part of my analysis where -- let me get this right.

There may be a part in my initial analysis where I said that there were papers that had -- that involved largely a higher dose than the cutoff that I made.

It's possible that some of those studies also included a lower dose as well. And so it's very hard to put those studies into a box because they do two things.

And so I may have referenced them in two or three different places.

BY MS. HUNT:

Q Okay. I'd like to look at what's been marked as Exhibit 267.

(Powell Deposition Exhibit 267 marked for identification.)

BY MS. HUNT:

Q And, Dr. Powell, you amended your report in this case, right?

A I did.

Q And would you say that the corrections you made were substantive?

MR. PADGETT: Object to form.

THE WITNESS: I don't know what you mean by "substantive," but I think they were important to make or I wouldn't have made them.

BY MS. HUNT:

Q Okay. And just to orient us in terms of the report with -- with apologies to Ray, just so I'm tracking where we are. This is page 33 of your report, which is marked as Exhibit 201.

And you say the majority of potentially relevant studies examined multiple outcome measures without corrections for multiple comparisons or accounting for false discovery rate, and then you have a string of citations; is that fair?

A Yes.

Q Okay. And we are going to talk a lot about multiple comparisons later today. I just want to focus on understanding your methodology for this piece.

Are you aware that there's another place in your expert report where you list a string of citations saying that the authors failed to correct for multiple comparisons?

A I am.

Q Okay. And that's in paragraph 91C, which is on

page 44 of your report.

A Say it again. I was looking at page 91.

Q Sorry. It's page 44 of your report.

A Got it.

Q Paragraph 91.

A Yes.

Q D. "Lack of correction for multiple comparisons."

So, same question: Beyond the changes, which we'll talk about in a moment, why were the citations different in paragraph 72 compared to paragraph 91D?

A I don't recall exactly. I mean, this is a section on some of the studies that had other reasons other than what I've stated before, and I may have duplicated that somehow and not included all the studies in the second version.

Q Okay.

A Possibly. I'm not sure how that happened.

Q And is a -- how is a reader going through your expert report supposed to know which studies you dinged for failing to correct for multiple comparisons?

A Well, any --

MR. PADGETT: Object to form.

You can answer.

THE WITNESS: What I would say is, again, if the goal was to have someone be able to do the same

analysis and come up with the same conclusions, or similar conclusions, or potentially a different conclusion, I would expect that they would do an analysis of all the papers that I've cited, and determine, in their minds, which one corrected or didn't correct for multiple comparisons adequately.

So I think that's how one would do that.

BY MS. HUNT:

Q Okay. And then I want to talk a little bit about the amendments that you made.

Is it fair to say that you removed a significant number of studies that you had initially said failed to correct for multiple comparisons from that list?

MR. PADGETT: Object to form.

THE WITNESS: Yes. Because when I looked at the initial 100 or 99 papers, I looked for -- I went through -- each time as I came across these different sections or bullet points, if you will, or lettered points, and I looked at those 100 papers to -- for multiple comparisons, comparisons, multiple FDR, false discovery rate, corrections, and used that as my initial criteria.

The reason I changed was because, at some point as I was reading the literature, it dawned on me that there are two ANOVA post hoc tests that actually

correct for multiple comparisons, even if it doesn't say in the article that they did that, and those are Bonferroni and Tukey's post hoc comparisons.

So out of an abundance of caution, I went back to correct the record objectively to ensure that I didn't include those -- I didn't want to include those in a correction for multiple comparisons.

What it is not -- what I didn't really ding a paper, if you use your terms for, is the fact that many papers do multiple ANOVAs across multiple types of studies, and just using the post hoc Bonferroni or Tukey test within each of those ANOVAs does not correct for comparisons across those ANOVAs, and in a conservative fashion, I decided that it would be better not to ding them for that because there is, as I understand it in a statistical world, some controversy or indecisiveness, I would say, about whether or not one needs to correct for that across ANOVA multiple comparisons or not.

BY MS. HUNT:

Q Okay. And if I'm understanding it right, when you did your initial review, you looked for words like multiple comparisons, comparisons, false discovery rate, in those studies; is that fair?

A Yes. And my expectation was that if you did the

corrections for multiple corrections, you would actually say that in your methods, and I realized at some point that that wasn't always the case.

Q Okay. Because really, the way you can tell if someone employed a statistical correction is by taking a look at the statistics, right? Like their p-value, their alpha value?

MR. PADGETT: Object to form.

THE WITNESS: Incorrect.

BY MS. HUNT:

Q Okay. Explain to me why I'm wrong.

A You can't look at their p-value and determine whether they corrected for multiple corrections. You just can't. There's no explanation.

You just -- it's not possible to look at a p-value and know whether or not they corrected for multiple comparisons.

You have to look at the methodologies they used to come up with that p-value, which is what I've done, and that's the result.

Q So if they --

A And I amended the report.

Q If they didn't use the word "multiple comparisons," did you assume that they just adjusted their p-value for some other reason?

MR. PADGETT: Object to form.

THE WITNESS: Adjusted their p-value. I'm not sure what you mean by "adjusted their p-value."

Sometimes when you do correction for multiple comparisons, or a so-called false discovery rate and you make multiple comparisons, then you do use a different cutoff p-value.

My recollection of these studies, many of these rodent studies, is that they did not change the p-value.

However, what they did do was use a Bonferroni post hoc test their ANOVA to draw comparisons among the multiple outcomes within a single, for example, behavioral domain, or within neurotransmitter measurements, or within amino acid measurements.

And so that's the way that one would look for that, and that's the way I ultimately did so.

BY MS. HUNT:

Q Okay. And so can you explain to me why -- let me make sure I have the name of this study. Give me one moment.

Okay.

Can you explain to me why Blecharz-Klin 2013 was removed -- I'm sorry, scratch that. This is what happens

when lawyers mess with statistics.

A What's the date on that Blecharz-Klin? I'm sorry.

Q It was 2013, but you don't need to look at it.

Dr. Powell, would you agree with me that there are over 40 changes in terms of individual studies taken out from that footnote?

A I couldn't agree to that because I don't know whether it's true or not.

Q Okay. If I represented to you that it's over 40, do you have any reason to believe that's incorrect?

A I believe that --

MR. PADGETT: Object to form.

THE WITNESS: I believe that I did not remove over 40 references from the -- any portion of the lack of correction for multiple comparisons in my document.

MS. HUNT: Okay.

THE WITNESS: So I'm not sure we're talking about the same thing.

BY MS. HUNT:

Q And all the changes that you made across -- across these amendments, none of them made you rethink your opinions in this case?

A Oh, I did re-evaluate my opinion in this case, but they didn't change the result of my opinion.

Q Okay. Do you explain anywhere in your amended

report how you re-evaluated your opinions?

A Do I explain how I re-evaluated my opinions?

Q In other words, after you found out that these scientists actually did correct for multiple comparisons, did you discuss anywhere why your opinion was still the same?

A I didn't explicitly say what -- the words that you're speaking of.

However, if you'll look carefully at paragraph 92, I analyzed, in the second iteration of my analysis, all the publications, leaving aside any of the experimental concerns, to see what was left in terms of consistently replicated believable results, and reached my opinion based on that, in large part, but also keeping in mind the concerns raised in the post hoc.

Q Okay.

A And so the basis of my opinions are there, and if it had changed my opinion, I would explain why, but since it did not, I didn't feel the need to explain why it didn't change my opinion because I didn't eliminate any of those articles in the second half of my analysis --

Q Okay.

A -- for any reason. Any experimental flaw, including multiple comparisons or false discovery rate corrections.

Q Okay. All right.

So moving a little bit deeper into your methodology, and I know you referenced this earlier, but it sounds like you went through sort of a long process, and I'm trying to understand that better.

So if we go to page 33 of your report.

Again, which I know we've spent some time here previously. You -- this begins a list of certain criteria that it looks like you had.

And I believe there are five of them. You know, the first is no correction for multiple comparisons. That's right in the middle of page 33.

And then you go on to say at the top of page 34: "Use of excessive drug doses."

And then slightly further down the page: "Use of adult animals," and then even further down the page: "Low number of animals."

And then finally on page 35, at the top, you say: "Absence of experimental replication."

Did I read that correctly?

A Yes.

Q Okay. And then if we go back to page 44, again, that section where you talk about non-relevant published studies.

Is it fair to say that there are more than five

criteria, starting on page 44, in terms of reasons you found a published study to be non-relevant?

A Yes. There are more than five that are listed.

Q Okay. I'd like to take a look at what I've marked as Exhibit 269.

(Powell Deposition Exhibit 269 marked for identification.)

BY MS. HUNT:

Q And so, Dr. Powell, just humor me here for my own benefit.

I took the liberty of listing out each basis you had for excluding a study as non-relevant.

And my question is: Which one is it, is it the list on page 33, or is it the list on page 44?

MR. PADGETT: Object to form. And I object to use of Exhibit 269 and 267 --

THE WITNESS: So on page 33 --

MR. PADGETT: -- to the extent, sorry.

Any suggestion they're accurate.

THE WITNESS: So on page 33, I'm generalizing. And in the following pages, I'm being excessively -- exceedingly specific.

BY MS. HUNT:

Q Okay. So is the list on page 44, the more specific list, is that the list that governs?

MR. PADGETT: Object to form.

THE WITNESS: Governs what?

BY MS. HUNT:

Q Why you excluded studies as non-relevant?

MR. PADGETT: Object to form.

THE WITNESS: I'll take a moment and just review the list to make sure I answer correctly.

MS. HUNT: I always like it when people check my homework, so please feel free.

THE WITNESS: It's not about checking you, it's just making sure that I understand every point before I answer.

So that is -- I mean, the list is in my report and those were things that I felt made them not relevant to the question at hand, which is, do relevant doses in rodent models lead to any evidence that's -- weighs in on causation or plausible biologic mechanisms.

BY MS. HUNT:

Q Okay. And I want to ask about some of the language in the criteria beginning on page 44, which is that second column on Exhibit 261.

(Powell Deposition Exhibit 261 marked for identification.)

BY MS. HUNT:

Q So criteria number 1, for example. "Findings confined largely to hepatotoxic higher doses."

Did I read that right?

A Yes.

Q Why did you use the word "largely" in that sentence?

A For the same reason I mentioned earlier, that some of the studies use both a larger dose and a potentially relevant dose, if memory serves. So I listed all those to point out the issue that with respect to those higher doses, that would make the -- it not relevant to the question at hand, which focuses, in my understanding, on typical recommended human doses, or the correlate of those in rodents.

Q Okay. And so if --

A So let me just back up a step, and say I'm listing parts of -- all the papers that had parts of them that are irrelevant. Some of them it's all of them, and in a list like this, it can be difficult to explain that.

And I've explained it here, and I've answered your question as best I can. Insofar as I put anything on this list that also uses a non -- that uses a dose that's relevant to the question, those papers were all considered in my analysis.

Q Okay. And --

A I want to be clear about that.
Q Thank you. Because that gets to my next question, and that is: If you had a study where you found that some of the doses were too high for you, but some of them administered what you would consider to be a therapeutic dose, you still considered the study or did you not consider it?
A I considered the portion of the study that --
Q That included the lower dose.
A That included the lower dose.
Q Okay.
A To my recollection, yes.
Q Okay. That's what was not clear to me.
So on -- on Exhibit 269, moving down.
I have the same question about the other highlighted language.
So, for example, number 9. "Less relevant outcome measures, no APAP alone group."
In that case, were the outcome measures somewhat relevant, just not as relevant as others?
A No.
Q Is there a reason you said less irrelevant instead of irrelevant?
A Yes. You know, I was being as conservative as I could be. And I guess a good example, I'm not sure if it's

even one -- if it's in that -- this part or another part, but there were some studies that looked at, for example, that I read. Anogenital distance as an outcome. And I don't consider that relevant to autism spectrum disorder or ADHD, per se, especially autism spectrum disorders, or ASD, because there's not a correlate. There's studies that don't show a correlation between anogenital distance and the diagnosis of autism spectrum disorder.

Q Okay.

A That's one example. Less relevant outcome measure of findings.

Why did I say less relevant? Because I was trying to be exceedingly cautious. And I'm aware of some of the potential hypotheses of mechanisms of action, and so I wanted to make it clear that, you know, I'm willing to consider those if they are relevant in anybody's mind.

Q And when you say "the potential hypotheses" there, are you talking about hypotheses that involve endocrine disruption and its effect on the developing brain?

A Among other things -- no. Actually, no.

I'm talking about studies that -- not studies that looked at effects on the developing brain, but studies that look at apex measures, such as anogenital distance, or perhaps a behavioral finding that, you know, is less relevant than the core behavioral findings that might be

relevant to ADHD or ASD.

Q Okay. But we wouldn't know necessarily why you found them less relevant unless we, I guess, entered control F and tried to search for those studies elsewhere in your report?

MR. PADGETT: Object to form.

THE WITNESS: I'm not sure because I don't remember exactly which of these references I've discussed in detail.

I can tell you that in my rebuttal report I focused on the 35 papers combined that were cited by Pearson and Cabrera. Yeah, Pearson and Cabrera, for the most part, although I looked at other studies that were referenced by other -- them and others.

MS. HUNT: Okay.

THE WITNESS: But I expect someone who is replicating what I've done to read the papers and decide for themselves what they feel is relevant.

BY MS. HUNT:

Q Okay. And number 10 on this list is "study of humans, not rodents."

And just so I understand, your systematic review was focused on the rodent in vivo literature, right?

A That's correct.

Q Okay.

A And I came up with, in my search, some studies in humans for some reason, and I tried to make it clear why those were not part of my rodent portion of my analysis.

Q You say in your Materials Considered List that you read Dr. Baccarelli's expert report and references.

A I'm sorry. Go ahead.

Q Does that mean that you read all of the epidemiological literature he cited?

A First of all, I don't think you accurately characterized the first statement, but I'd love to look at it because I'm not sure if I've -- could you point me to where I said that?

Q Yeah, absolutely. So if we go to page 125.

A Of my report?

Q Of your report, which is marked as Exhibit 201. You'll see it's item 250.

It says: "Report of Andrea Baccarelli, M.D., Ph.D., MPH, including references and exhibits."

A And what that means is I read through her reference list and I read the exhibits associated with her report.

Q Got it.

A Now, the answer to your question, though, is: I read multiple epidemiologic studies in preparation to understand the context of the entire review of the

literature and the report that I generated.

Q Okay. But the epidemiologic literature you read was not part of your systematic review, fair?

A Correct. It only provided context for my systematic review of the rodent/acetaminophen literature, and the question of rodent studies and their impact on potential biologically plausible mechanisms and/or cause.

Q Okay. And are you aware that there is an epidemiologist who is going to testify on behalf of the manufacturers of acetaminophen in this case?

A I think so, yes, but I don't remember which one is which, but I'm aware that there are epidemiology experts on both sides.

Q Okay.

A To the best of my knowledge, yes.

Q Have you read that report?

A Which report?

Q I believe the expert --

A Whose report, how's that?

Q Okay. I'll back way up.

Are you aware that Dr. Pinto Martin is an epidemiologist who's going to be a testifier on behalf of the manufacturers of acetaminophen in this case?

A I'm aware that he is an expert witness on the defense side of this case. And I have read that person's

report.

Q Okay. And is there a reason you didn't rely on it in forming your conclusions?

A Of the rodent literature? Yes.

MR. PADGETT: Object to form.

BY MS. HUNT:

Q Okay. And that's because your -- your expert report is focused on the animal and the rodent literature, right?

A It is.

Q So that's why you didn't rely on Dr. Pinto Martin?

A Well, everything that I relied on is referenced, including, I hope, Dr. Pinto Martin's report.

And if it's not on there, then it's an oversight on my part, but I did read all the reports of all of our and your experts.

Q Okay.

A If that's your question.

Q But did you rely upon it in forming your ultimate conclusions in this case?

A For context to some degree.

Q Okay.

A But not -- it doesn't -- it's not part and parcel of reviewing the rodent literature to look at the human literature.

Q Do you say anywhere in your -- either your expert report or your amended expert report that you read or that you relied on Dr. Pinto Martin's report?

MR. PADGETT: Object to form.

THE WITNESS: I don't recall.

BY MS. HUNT:

Q Okay. Going back to your expert report. On page 97, you start a section 2 that says: "Dr. Hollander's and Dr. Baccarelli's opinions regarding the purported biological mechanisms identified by other plaintiffs' experts are not supported by the specific literature they cite."

Did I read that reasonably correct?

A I'm trying to catch up to where you are.

Q Sorry.

A This is paragraph 223?

Q Yes.

A Where it starts: Dr. Hollander's and Dr. Baccarelli's --

Q I just read heading 2, that's right above --

A Oh, sorry.

Q Right above 223.

A Yes. You read that correctly.

Q Okay. And is it fair to say that the studies that you discuss in paragraphs 223 through 227 are human studies?

A Some of them, I guess, yes.
Q Can you point to any that are animal studies?
A I could -- I don't know if I can or not, but if you want me to go through each one, which I don't think is worth our time, as we sit here today, I'll say that I have no knowledge that what you said isn't true, that they're. all -- they may all be human studies.
Q Okay. And so to the extent that you evaluated these human studies in those paragraphs of your report, is that outside of your systematic review?
MR. PADGETT: Object to form.
THE WITNESS: That's an interesting question.
I performed a systematic review, and then in rebuttal to the plaintiffs' experts, I read, in detail, each of these papers for evidence that they supported the conclusions for which they were referenced.
And I didn't find that those same papers led me to the same conclusions.
BY MS. HUNT:
Q Did you --
A So I don't know if that's -- is that a systematic review? I systematically read the papers but, you know, I didn't do a -- the same thing that I did in the beginning of my report.
Q Okay. And you said that you didn't find those

same papers led you to the same conclusions.

In your work, is it common for scientists to interpret data differently?

MR. PADGETT: Object to form.

THE WITNESS: Is it common for scientists to interpret data differently?

I would say that different people -- different scientists can reach different conclusions looking at the same literature.

However, what I would say is that oftentimes many of the discussion points and conclusions are qualified by "may" or "suggest" or "might" or "not inconsistent with," and to the extent that those are speculative discussion points, or, if you will, conclusions, I would say that there's often not a major disagreement among them when you take into account those qualifiers.

BY MS. HUNT:

Q Could you have done a separate literature search on acetaminophen and biomarkers in human studies?

MR. PADGETT: Object to form.

THE WITNESS: I have access to literature searches, and I could do lots of them.

MS. HUNT: Okay.

THE WITNESS: I can tell you that I reviewed

and read, again, which I've said before, many, if not all, of the epidemiologic studies in humans.

And I'm certain that I didn't read every biomarker study of acetaminophen's effects, especially with respect to the liver and non-brain organs.

BY MS. HUNT:

Q Did you do a Bradford Hill analysis, or any other weight of evidence analysis, to review these human studies?

A I reviewed the human studies and took into consideration many of the concerns and flaws that I noted independently -- before -- when I read those papers, before reading any of the reports, before I had any of the reports, and I had many of the same concerns about those epidemiologic studies.

For example, many of them don't use ASD diagnosis or ADHD diagnosis as an outcome measure, which struck me as odd and concerning.

And then, second, they -- most, if not -- most of the studies don't do anything to account for what I call the elephant in the room, which is that 75, 80 percent or more of both ASD and ADHD, are caused -- known to be or thought to be, by consensus, caused by genetic changes. And so that struck me as odd.

And so I didn't feel -- and I didn't feel like there was evidence to suggest causality in humans.

Now, in the end of the day, I looked and read the expert reports and found that my thinking was in line with a portion of the epidemiologists that reviewed those same studies.

MR. PADGETT: We've been going for an hour and 20.

MS. HUNT: Yeah. Two more minutes, and then I'll be done.

BY MS. HUNT:

Q Dr. Powell, do you agree with me that the epidemiology in this case is high quality?

MR. PADGETT: Object to form.

THE WITNESS: Which epidemiology?

BY MS. HUNT:

Q Well, you said you reviewed nearly all the epidemiological literature on this issue.

So I'm just wondering, do you feel like the literature you reviewed was of high quality?

MR. PADGETT: Same objection.

THE WITNESS: All told, I don't believe that they all accounted for or controlled for the most important potential confound, which is the fact that genetic changes caused the vast majority -- or thought to cause the vast majority and agreed upon to cause the vast majority of autism spectrum disorders and ADHD.

As to the quality of the studies, it didn't -- it didn't escape my notice that in some of the studies, there were multiple, multiple measures in multiple -- and different checklists and screening, nondiagnostic measures, and that some of the studies didn't correct for multiple comparisons, as far as I could tell.

And that has been borne out by, I think the reports of at least some of the epidemiologists.

BY MS. HUNT:

Q So, so to go back to my question. You would not agree that they are high-quality studies?

MR. PADGETT: Object to form.

THE WITNESS: It depends on how you view them. If you're -- if you're viewing them as a study that's going to lead to a conclusion of causality, and as far as the diagnosis of ASD and ADHD, I would say that many of them were not high quality for that outcome measure.

BY MS. HUNT:

Q Would you say that they came from large and impressive datasets?

MR. PADGETT: Object to form.

THE WITNESS: Some of them came from large datasets, and all the incumbent issues, problems and

concerns with such datasets and limitations, were inherent to those studies, so, yes.

MS. HUNT: We can take a break.

THE VIDEOGRAPHER: Off record. 11:04 a.m.

(Off the record at 11:04 a.m.)

THE VIDEOGRAPHER: On record, 11:23 a.m.

BY MS. HUNT:

Q Okay. Dr. Powell, I want to go to page 35 of your report, which has been marked as Exhibit 201.

And there is a header that says: "Absence of Experimental Replication."

Did I read that correctly?

A That's what it says, yes.

Q Okay. And you say right beneath that: "Experimental replication is the foundation of scientific truth. In fact, no scientific finding makes it into the textbook as a fact without replication by others."

Did I read that correctly?

A You read that introductory sentence to this section correctly, yes.

Q Okay. And as you were preparing your expert report, did you check to see if findings by scientists about acetaminophen and neurodevelopmental disorders had made it into any textbooks?

A No. I'm not aware of actual textbooks on autism

and ADHD textbooks, like you would use to teach undergraduates or graduate students, but I did not.

Q Okay. So you're not aware that several major textbooks on pharmacology, for example, have included data on the link between acetaminophen and neurodevelopmental disorders?

MR. PADGETT: Object to form.

THE WITNESS: I wouldn't doubt that there are text -- there are books that have been published that review literature and make speculative comments about what a certain study may or may not mean, what's in the realm of possibility, just like any discussion part of a paper.

(Powell Deposition Exhibit 223 marked for identification.)

BY MS. HUNT:

Q Okay. I'd like to give you what I've marked as Exhibit 223.

And, Dr. Powell, this is what you cite in your -- in your expert report for the premise that a study has to be replicated in order to be relevant. Fair?

A No. I don't think it is.

Let me look.

Q Okay. Well, let's go back to your expert report.

A For example, the first paragraph starts the same

as what I've quoted, but it doesn't end the same way as I've quoted. Just to name one --

Q Okay. So --

A -- difference.

Q If we go to your expert report on page 35, where you have that block quote, are you saying that that block quote is altered from the quote that's on this website?

A No.

Q Okay. Can you explain to me what you mean?

A This was copied and pasted from the website at the link credited -- it's credited to underneath it.

I don't know what you're looking at, but that's what I'm looking at.

Q Okay.

A In fact, your link is different than mine. The link at the top of your page of your exhibit, 223, is it?

Q Yes. Okay. So your --

A It's different than mine.

Q Your -- your position is that this is not what you cited?

A My position is that I copied and pasted this from the NIH website listed here, and our two links are different.

Q Okay. And so you think I -- I have the wrong link; is that fair?

A I don't know whether you have the right or the wrong link, but this was the information that I copied and pasted from the website verbatim at the time that I wrote my -- put this -- wrote this part of my report.

Q Okay. And is there a reason that you cited to this website as opposed to like a peer-reviewed academic article?

A Yes.

Q Can you explain what that reason is?

A Sure. As I point out in the report, this is a fundamental tenet of interpreting science.

Many publications report striking, earth-shattering results, that don't stand up under further scrutiny, and that's how science works. It's an iterative process. So it's absolutely critical.

And NIH requires that we teach these things to graduate students, we teach it to undergraduate students, and so I take it as a broadly, well-known fact, that reproducibility, in independent labs especially, is a critical part of the scientific process when one is interpreting the literature.

Q Okay.

A And so I don't think it bears the need for -- I mean, all of your experts on your side and ours talk about consistency of the findings as critically important, period.

Q Okay. And so you don't recognize the exhibit that I have marked as 223?

A I didn't cite any -- what -- all of -- I didn't -- I only cited -- I cited one sentence in common with this report, and it's the first sentence under "Enhancing reproducibility through rigor and transparency," and it has a sentence that starts: "Two of the cornerstones of scientific advancement for rigor in designing and performing scientific research and the ability to reproduce biomedical research findings."

Q So is it your position that if I typed in the URL at the bottom of that block quote, I would not end up at the website marked as Exhibit 223?

A No, I have no idea what you would come up with if you did that now because they may have changed their website since I took this off of there.

Q Okay.

A But I didn't make it up. I can assure you of that.

Q Oh, I'm -- I might accuse you of many things but that's not one of them, Doctor, so don't worry.

A And, just likewise, I'm not accusing you of having somehow engineered a difference of documents.

Q Assuming for purposes of the deposition that this is the resource that you cited to, would you agree with me

that the -- the website in Exhibit 223 is largely about transparency?

MR. PADGETT: Object to form.

THE WITNESS: I'm sorry, which -- you're referring to my report or this website? I'm confused.

BY MS. HUNT:

Q This website, Exhibit 223.

A Would I agree that this is largely about that?

Q About transparency.

In other words, the point of this website, as I understand it, and I want to know if this is inconsistent with the way you understand it.

The point of this is to make research more transparent so that others can reproduce it, right?

MR. PADGETT: Same objection.

THE WITNESS: That is one of many purposes of what I haven't read, which is this entire document.

BY MS. HUNT:

Q Okay. Take your time and take a look at it. I can wait.

A Oh, there is. "When a result can be reproduced by multiple scientists, it validates the original results and readiness to progress to the next phase of research."

This is -- well, and that's one of the sentences, I think, that I quoted.

And I didn't engineer this with selective sentences from here and there. This was, I think, verbatim from that website, as far as I recall.

Q Okay. So this is --

A Or a website.

Q So this is the website you cited?

A No, I didn't say that. I cited the website that I cited underneath the block quote, period.

Q Okay.

A So -- and to the extent that this doesn't have a paragraph that matches mine, this is not the website that I quoted.

Q Okay. Is there anything on this website that's specific to toxicology?

A This is about science and toxicology is science.

Q And --

A So, yes. It's specific to toxicology, which is a part of the subset -- it's a subset of all science.

Q So this website that you printed off from the NIH, your opinion is that that applies equally to every area of science -- every area of science, even if it's not specifically discussed?

A Well, I disagree that I printed this off, but to the extent that I copied and pasted from the NIH website what I've cited, reproducibility is important in every

branch of science.

Q Okay.

A Period.

Q Is reproducibility the same as whether a study has been reproduced?

MR. PADGETT: Object to form.

THE WITNESS: So there are many types of reproducibility and replication.

One is, there's independent replication under different circumstances in a non-overlapping laboratory, and then there's replication within a laboratory.

BY MS. HUNT:

Q But isn't reproducibility just the ability to reproduce a study?

A No.

Q In other words -- it's not?

A Not just that, no. It isn't.

For example, if I studied nuclear fusion or superconducting activity of a metal under room temperature conditions and I did it twice and I published it twice, that would be replicated and not independently replicated, and if no one else could reproduce that result, it would be problematic, and you wouldn't reach the conclusion that it could be done at this point in time.

Q Okay.

A That's been all over the press lately, among other examples.

Q But part of reproducibility is just transparency, right, so that another scientist can go behind you and try to do the same experiment?

MR. PADGETT: Object to form.

THE WITNESS: I wouldn't say that. I wouldn't agree with that fully.

I would say that if one is complete and transparent in their reporting of their methodologies, then the research should be replicated and replicable, and until it is, it's just oneoff finding.

BY MS. HUNT:

Q Okay. I'd like to move back to page 14 of your report, which we've marked as Exhibit 201.

And in paragraph 36, in the bottom half of that page, you talk about the ARRIVE 2.0 guidelines, and you say: "Scientists have generated a set of accepted guidelines for performing and reporting scientific experiments known as ARRIVE 2.0."

Did I read that reasonably correct?

A Yes.

Q Okay. And I'd like to give you a copy of those guidelines, which we've marked as 259.

(Powell Deposition Exhibit 259 marked for identification.)

BY MS. HUNT:

Q Do you use the ARRIVE guidelines in your own work?

A To a degree.

Q Explain that a little bit more.

A Well, I would say that I try my best to provide the methods in all of my publications in a way that they can be reproduced by others.

I do exploratory research, and I would say that we're looking for potential end roads into findings that might be relevant to a genetic -- a gene's changes in the brain and subsequently a mouse's behavior.

So we don't necessarily, in every paper that I've ever published, do every single thing that's in this July 2020 report in every paper in our exploratory research in animals.

Q And so is it possible for a study to still be relevant to a field of research, even if it doesn't meet every single ARRIVE 2.0 guideline?

MR. PADGETT: Object to form.

THE WITNESS: I would say that in my analysis, I have considered every finding of every paper, regardless of any of the scientific flaws or criticisms, and regardless of their compliance with the

ARRIVE guidelines, or any other guidelines in reaching my opinions.

And so that's what I do.

BY MS. HUNT:

Q Okay. So I think you may be answering a different question than what I'm actually asking, but I'm asking -- we were talking not about this case, but about your work out -- outside of being a paid expert, and what I asked was: Is it possible for a study to still be relevant to a field of research, even if it doesn't meet every single metric in the ARRIVE 2.0 guidelines?

A Possible, yes.

Q Okay. And, in fact, some of your own work has not met every single ARRIVE 2.0 guideline, correct?

MR. PADGETT: Object to form.

THE WITNESS: I don't believe they all have, correct.

BY MS. HUNT:

Q Okay. And is it your understanding that the ARRIVE 2.0 guidelines are meant to be a methodology to evaluate causation in the context of the safety of a compound?

A That's not how I've applied those guidelines, and, no.

Q Okay.

A It's not specifically for that purpose, especially with regard to rodent studies and their impact on causality, which is how -- where I've specifically applied Gurusamy's guidelines on translatability of rodent findings to humans and these reporting guidelines.

Q Okay. So if we go to your expert report at -- which is marked as Exhibit 201, at page 30 -- I'm sorry page 29, we'll start there.

So it says: "Results of systematic review," and I think we mentioned this language earlier: "Of the 99 peer-reviewed original research publications evaluated a detail, only two publications passed criteria for relevance to the condition of concern and appropriateness of experimental design and statistical analysis. These guidelines included whether studies used animals, a relevant dose, the relevant timing of drug administration, appropriate statistical methods, a relevant outcome measure."

Did I summarize that reasonably accurately?

A For the most part. And I would just point out that if you want to read the summary of my finding in this systematic review, I would point you to paragraph 93.

Q Don't worry, I'll get there.

A Good.

Q But thank you.

So then you continue on in the next paragraph to say: "Two papers passed criteria for relevance to the condition of concern and appropriateness of experimental design and statistical analysis."

And then -- when you said: "Experimental design and statistical analysis," you refer us back to paragraphs 37 and 38 of your report. And those are, again, back at page 14 and -- 14 through 16, where you talk about the ARRIVE guidelines?

MR. PADGETT: Object to form.

THE WITNESS: I'm not sure that's an accurate statement.

I would say that I listed some of the ARRIVE guidelines. If you're curious to know where -- what my criteria were in this systematic review, I would point you to the detailed issues in the pages that I'm trying to find.

The initial ones you quoted, right, so --

BY MS. HUNT:

Q So the ones on page 44 --

A 34.

Q Oh.

A It starts on page 33 and goes to paragraph 93 on page 46.

Q Okay. And so --

A I believe, I think. Well, maybe it goes a little bit to 92, but before 92.

Q So we can agree that you didn't use the ARRIVE guidelines really as part of your systematic review. It's more something you mention in terms of a study design quality?

A I believe I've explained --

MR. PADGETT: Object to form.

THE WITNESS: I believe I've explained in detail the methodology that I used and I went through, and I explained that I didn't include all of the ARRIVE guidelines because in some cases I thought the papers generally did a good job of them, for example, blinding investigators of the treatment group of the animals while performing and analyzing the experiment.

So I didn't find it necessary to include that as a factor because most of the studies did that. So it wasn't a problem. Communicating he was aware of group allocation at different stages of the experiments.

You know, were they all perfect at that? No, but I don't consider that as important as other things I looked at and listed in detail.

BY MS. HUNT:

Q Okay. So it's fair to say that your systematic

review departs from the ARRIVE guidelines where you felt it was appropriate?

MR. PADGETT: Object to form.

THE WITNESS: I would say that it is an amalgam of Gurusamy, et al., and the ARRIVE guidelines, and my own list of what I think was most important and critical in terms of scientific experimentation.

BY MS. HUNT:

Q And so would you say that that amalgamation, as you described it, is that methodology published anywhere?

A Gurusamy and all over the ARRIVE guidelines.

Q I'm talking about the Dr. Powell methodology. The amalgamation that you talked about.

A I could say that every single factor that I've considered is published in the literature independently many times over.

Q Okay. But in terms of these are the criteria to evaluate a neurotoxicological endpoint, there's no study that says these are the criteria you look at?

MR. PADGETT: Object to form.

BY MS. HUNT:

Q That match yours?

MR. PADGETT: Same objection.

THE WITNESS: Again, Gurusamy overlaps with

my criteria, and I've conservatively conceded, if you will, that these papers have met some of these guidelines, of the ARRIVE guidelines, but not all of them.

MS. HUNT: Okay.

THE WITNESS: But I don't find them to be particularly important for critical flaws like the others that I've listed.

BY MS. HUNT:

Q Okay. I want to talk to you a little bit about numbers of animals in these studies.

Is it fair to say that you dinged a number of studies for having low numbers of animals?

MR. PADGETT: Object to form.

THE WITNESS: First of all, I want to say that you keep using the word "dinged." I never eliminated or excluded any study in my overall analysis, period.

And that's stated explicitly on paragraph 90 some odd -- 93, I believe it is, or somewhere in the low 90s.

And I considered every single study irrespective of any of their potential flaws, but I felt it was important to detail those flaws for the reader.

And I would say that -- I've forgotten the second part of your question.

BY MS. HUNT:

Q That's okay. I'm not -- I'm not sure you were working off my question.

A Oh, I was working off the first statement of your question. If you can repeat it or have it read back, I'd be happy to address that.

Q Okay. Is it --

A That testimony, excuse me.

Q Is it fair to say that you criticized a fair number of studies for having low numbers of animals?

A Oh, I pointed out that some studies had lower animal numbers than is specified in Tyl 2008, by Dr. Rochelle Tyl, which is relied upon by at least two or more of your witnesses in detail, where it says that one needs to have an in of 10 animals per sex, at least, in every dose in both behavioral and pathologic studies.

Q And --

A I think that's almost a direct quote, but it's a paraphrase.

Q Did you rely on Tyl 2008 in your methodology otherwise?

A I relied on my experience as someone who has been studying animal models for over 30 years in neuroscience and

over two decades in the field of neurodevelopmental disorders, such as autism spectrum disorder, intellectual disability, among others.

And so what I will say is, I've done these power analyses myself, and for behavioral experiments in particular, an in of less than 10 is unacceptable.

I also relied on Silverman, et al., which states that you need to have an adequate power and adequate ins.

And, for the record, in my studies, we use ins of 20 routinely for our behavior.

Q Okay.

A But, no, I didn't rely on Tyl 2008, but your experts do.

Q And is there a reason that you decided that Tyl 2008 was not a helpful guidance document in terms of evaluating neurotox endpoints?

A Well, I never said that.

Q Well, then why didn't you use it?

A Because I hadn't read it and it didn't come up in my literature search. It came up in my report after I read the toxicology experts on the plaintiffs' side.

Q Okay.

A And so I read it carefully because I wanted to know what it said and why they thought it was so important as to reference it multiple, multiple times, to defend

things that I feel are less -- virtually indefensible.

Q Okay. You mentioned Silverman 2022.

I'd like to take a look at that. I've marked it as Exhibit 258.

(Powell Deposition Exhibit 258 marked for identification.)

THE WITNESS: I don't think that's it. Whoever's pulling this up, I don't think you have the right document.

MS. HUNT: Okay. Thanks for your patience. Here's your copy.

THE WITNESS: Thank you.

BY MS. HUNT:

Q Okay. So this is one of the studies or papers that you relied upon in forming your opinions, right --

A Myself --

Q -- Dr. Powell?

A I'm sorry. Myself as well as your experts, correct.

Q That's right.

MS. KAPKE: What's the exhibit number?

MS. HUNT: It's 261, I apologize.

BY MS. HUNT:

Q And Dr. Powell, was this paper the result of a round table that took place?

A I would say it was the result of multiple meetings among the authors --

Q Okay. And were you --

A -- my understanding.

Q Were you involved in those meetings?

A I was.

Q And is there a reason you chose not to sign your name to this paper?

A Yes.

Q Can you tell me what it is?

A No.

Q Why?

A Because I'd rather not.

Q Okay. Well, this is my deposition and --

A I understand.

Q -- I'm entitled to an answer, and you're under oath, so I'd like to know the reason.

A With the caveat that this is -- this should be marked as highly confidential information because it's very personal.

I thought that the writing style was not appropriate. And I don't think it was -- I don't think that every single thing in this paper was under my control personally, because there were issues that I had, you know, group think was going to trump, and so the stated reason is

because I have plans to write my own similar review.

Q And so is it safe to say you relied on a paper which has an inappropriate writing style and the contents you don't agree with in order to attack the opinions of the plaintiffs' experts in this case?

MR. PADGETT: Object to form.

THE WITNESS: I don't think I attacked anyone's opinions, I rebutted them, number one.

And number two, I read this paper, I agree with many of their suggestions, but not all of them.

BY MS. HUNT:

Q Are you aware that this paper is specifically about genetic models of ASD?

A That's an interesting question.

MR. PADGETT: Object to form.

THE WITNESS: I don't know that it's -- I can't remember, to be honest.

BY MS. HUNT:

Q Okay. Well, why don't we look at the page that's marked as 261.4. It's page 4 of the document, and under 1.2, on the left-hand side, you can see some highlighted language there.

"We focused on genetic rather than environmental factors because of their higher potential for inter-laboratory reproducibility and their known construct

validity."

Did I read that reasonably correctly?

A You read a sentence correctly that describes what articles were used to reach these conclusions and the suggestions are what they learned.

Q Okay. And is it fair to say that in --

A But I would dis -- I'm sorry. I would disagree with the idea that these sorts of suggestions wouldn't apply to animal models of other -- of other types.

Q Okay.

A They relied on the most inter-laboratory reproducible and construct valid studies is what they say here.

Q And you've already testified under oath to this jury that you've never performed an experiment involving determining if a substance causes a change in neurodevelopment, right?

A That is true.

Q And -- okay.

Moving back more broadly to the number of rodents in a particular study.

Is it your opinion that the number must be the same regardless of the endpoint that's being studied?

A No. One has to -- should do a power analysis to determine the number of animals, especially if you're going

to use this study to make major decisions about humans, number one.

And, number two. I don't think it's necessary to have a high in if you're doing an exploratory study that you're going to follow-up on in detail to actually decide whether it's true or not, or scientifically accurate or not.

Q Okay. And there are certain endpoints, like, for example, evaluation of histology or neurochemical analysis where you might be adequately powered with a much lower number of animals, right?

A It's possible --

MR. PADGETT: Object to form.

THE WITNESS: It's possible, although I'll point out that Tyl 2008 states very clearly that an in end of 10 of each sex for each dose in a toxicology study is important for both behavioral outcomes and pathologic outcomes.

MS. HUNT: Okay. I'm at a good stopping point for a break, and I think lunch is here.

THE WITNESS: Lunch?

THE VIDEOGRAPHER: Off record. 11:54 a.m.

(Off the record at 11:54 a.m.)

THE VIDEOGRAPHER: On record. 12:44 p.m.

MS. HUNT: Okay. All right, Dr. Powell. We were talking about this a little bit earlier.

This is Exhibit 229. And let's just take a look at the title.

(Powell Deposition Exhibit 229 marked for identification.)

BY MS. HUNT:

Q It says: "Identification and interpretation of developmental neurotoxicity effects."

Did I read that reasonably correct?

A You did.

Q Okay. And does it appear to you that this article is specifically about developmental neurotoxicity?

A It's related to that. I can't remember if it's in humans exclusively or rodents as well, I'm not sure.

It looks like there's a selection of animal models so, yes, it is, you're correct.

Q Okay. And I think you said earlier that this article didn't come up in your search of the literature, right?

A The way I searched the literature, I didn't -- I don't recall seeing it, no.

Q Okay. And that you read this article for the first time after you saw plaintiffs' expert reports?

A I believe that's correct.

Q Okay. And I think you pointed out some comments that Dr. Tyl makes in this article about the number of

animal subjects that are appropriate for a given experiment.

Do you recall that testimony?

A I do, yes.

Q Okay. So I'd just like to spend a moment looking at that in more detail to make sure we have the full context.

If you turn to the page that's been marked as 229.3, and then go to the lower left-hand corner of that page, there's a heading that says: "Gender and number of animals."

And it says: "Ideally, the number of animals within each experimental group used in a developmental neurotoxicity study should be guided by the known variability of the test methods and procedures used to measure the various study endpoints. However, a test to establish a single number of animals as the group size for all tests and procedures carried out throughout the study, based strictly on the variability of the test method or procedure, becomes very complicated, if not virtually impractical."

Did I read that correctly?

A That's what it says here, yes.

Q Okay. And then she goes on to say: "EPA guidelines recommend that there would be a number of 10 per sex or 20 pups per dose for the behavioral and pathological

endpoints."

Did I read that correctly?

A You did.

Q Okay. And that was the part you were talking about earlier, right?

A Yes.

Q Okay. And then I'd like to look just a little more deeply at this article.

If we could go to the page marked 229.22. If you're following the page numbers from the journal, it's page 370.

And there's a section header on the left-hand side of the page called: "Weight of evidence approach to interpretational study data."

Are you with me?

A Yes.

Q Okay. And in the second paragraph of that section, it says: "This paper and its authors are not the first to struggle with how to interpret developmental neurotoxicity data."

And I want to stop for a moment and ask you, is it fair, in your opinion, to say that developmental neurotoxicity data is pretty complicated?

MR. PADGETT: Object to form.

THE WITNESS: That's too broad and vague for

me to answer, but what I can say is that we're talking about a couple of different things, and I want to make sure I understand the subtext here.

Developmental neurotoxicity is a separate issue from the question at hand, which is, does acetaminophen, given during the rodent equivalent of human gestation, cause autism spectrum disorders or -- and/or ADHD, and is there a plausible biological mechanism. That's important.

And so I want -- I can't answer unless we clarify what we're talking -- which of those two things we're speaking about.

BY MS. HUNT:

Q So, do you not understand that evaluating the rodent literature on the effects of acetaminophen on neurodevelopment inherently involves interpreting developmental neurotoxicity data?

MR. PADGETT: Object to form.

THE WITNESS: Again, I would need to know if you're referring to -- as relevant to this case, or simply a screen for a developmental neurotoxicant, which is a different matter altogether.

BY MS. HUNT:

Q I'm asking you in general. Do you agree that data around developmental neurotoxicants is complicated?

MR. PADGETT: Same objection.

THE WITNESS: I don't know what that means, developmental neurotoxicants, with respect to its application to this case.

I would say that science is complicated and insofar as neurotoxicological studies, or developmental neurotox studies, as they talked about here, is a subset of that science, that is complicated.

BY MS. HUNT:

Q So do you think all areas of science are equally complicated?

A I would say that all -- all science are equally complicated. Well, it depends on who the person is, right?

So I'm not a physicist. So I find physics research incredibly complicated, and I find genetic animal model and neurotoxicological and epidemiologic studies of mice to be much less difficult than physics research, for example.

Q So sitting here today, you're not willing to agree that developmental neurotoxicology is a complex field of science?

A I would say science is complex for any lay person, and it's hard to explain, but I don't think it's rocket science to analyze neurotoxic data or data on models of epidemiological exposures, as a scientist, who's been

trained to work with animal models of neurodevelopmental disorders.

Q Right. And that's why you feel comfortable doing it, even though you've never undertaken a developmental neurotoxicity study?

MR. PADGETT: Object to form.

THE WITNESS: I feel comfortable evaluating this literature and many other types of literature.

MS. HUNT: Okay.

THE WITNESS: All of which are complex.

Some of which aren't directly related to exactly what science I do in my lab on a day-to-day basis.

BY MS. HUNT:

Q Okay. So when --

A I've never done a stroke study, for example, but I routinely look at the literature on stroke and many other neurologic topics and evaluate those studies.

Q So when Dr. Tyl says at the beginning of that paragraph: "This paper and its authors were not the first to struggle with how to interpret developmental neurotoxicity data," they just don't understand it as well as you?

MR. PADGETT: Object to form.

THE WITNESS: That's not at all what I said.

BY MS. HUNT:

Q Okay. So why do you think it would be a struggle to interpret that data?

A Well, that's an interesting question. I would say that it would be a struggle for many reasons.

One being that, you know, when you're -- you want to have consistency. You want to have reproducibility. You want to have rigor, statistical rigor, and you want to do a dose-response curve and you want to use the appropriate statistics and, you know, it's -- then at some point you may want to actually consider what the implications of those findings are for human beings and that can be a struggle for sure.

Q Okay. And she continues later in that paragraph to say: "There are a number of papers that specifically discussed interpretation of developmental neurotoxicity data. All of these previous papers, and this paper, have used a weight of evidence approach."

Did I read that reasonably correct?

A No, not at all. It says: "There are a number of previous papers that involved interpretation of adult neurotoxicity data. And involve" -- and I'm going to say that -- that also -- the next part, is: "And involved also the weight of evidence approach."

So there are one, two, three, four, five, six

studies referenced, and those are six studies that involve interpretation of adult neurotoxicity data using a weight of the evidence approach.

That's what it says.

Q Okay. Sir, I think we're talking about two --

A And that's what I think it means. No.

Q Two different -- I'm asking you, please, to be respectful and not interrupt me, and I'll do the same and be respectful and not interrupt you.

A I appreciate that.

Q If you need to take a deep breath, that's totally fine, but I'm talking about the last sentence of that paragraph. Okay?

So let me know when you're with me.

In addition -- and this is the piece talking about developmental neurotoxicology, okay?

"In addition, there are a number of papers that specifically discussed interpretation of developmental neurotoxicity data. All of these previous papers and this paper have used a weight of evidence approach."

Did I read that reasonably correct?

A Yes. It -- and to interpret that, it describes six papers, and that's the approach they used.

Q Okay. And did you take that into account when you were deciding on which methodology you were going to use?

A I took into account my own understanding of -- my 30-plus years of training and evaluating the literature of rodent behavior, electrophysiology, protein data, RNA data, and behavioral data.

And my understanding of autism spectrum disorders and other neuropsychiatric, neurodevelopmental disorders wrote in the literature, and I came up with my own list of important things, and I compared that to Gurusamy, et al., and I compared that to the ARRIVE 2 guidelines.

I was lenient in deciding that some of these were not so important, and I eliminated them.

Q Okay. So I'm going to ask my question again.

Did you take into account this fact pointed out by Dr. Tyl that all of the papers -- let me go back, because I want to make sure I get the language right.

That all of the papers she reviewed specifically discussing interpretation of developmental neurotoxicity data, all used a weight of evidence approach.

Did you take that into account?

MR. PADGETT: Object to form.

THE WITNESS: I did not take into account that there are six papers cited, that all six of them used the weight of the evidence approach.

And not all papers that review these findings use a weight of evidence approach, and that's implied

by the sentence in my opinion.

BY MS. HUNT:

Q Okay. And I'd like to move now to the page that's marked as 229.24. If you're following the journal numbers, it's page 372.

A I think I'm there.

Q Okay. And it's in the bottom left corner under "Consistency."

And, Dr. Powell, you'd agree with me that this is the section in which Dr. Tyl is talking about the consistency of effects between studies, correct?

Take your time.

A Okay. Yes. This has something to do with consistency.

Q Okay. And at the end of that paragraph, Dr. Tyl says: "Lack of information about a biologically relevant pattern should be considered as an uncertainty and not a negative in a weight of evidence evaluation. Lack of a known underlying biological explanation or mechanism is not a reason to discount the findings."

Did I read that correctly?

A You did.

Q Okay. And do you agree with that?

A First, I'll have to interpret what I believe that it means.

Q Feel free.

A Lack of information about a biologically relevant pattern.

So what I believe -- I'm assuming that refers to is above in the first part of the -- this section, they're talking about if changes in an endpoint are observed only at one age, they might be considered of limited significance or biologically relevant and the pattern is consistent with the ontogeny of the endpoint, especially if the changes are associated with a similar pattern in other endpoints like, e.g., if there were also developmental delays and a number of other developmental endpoints indicating likely overall delays in development.

So I believe the first sentence is referring to that. And it's an uncertainty and not a negative in the weight of evidence evaluation. I don't know what she means by negative in the weight of evidence evaluation.

I don't think she means Dr. Pearson's approach, or saying a study is either causative or negative in support of a conclusion.

"Lack of a known" -- and then the sentence: "Lack of a known underlying biological explanation or mechanism is not a reason to discount the finding," and remember, we're talking about a finding, not being discounted.

We're not talking about anything more than that.

Q Okay. I would like to show you what has been marked as Exhibit 270, Dr. Powell.

(Powell Deposition Exhibit 270 marked for identification.)

BY MS. HUNT:

Q Dr. Powell, and is this the Gurusamy article that you, I think, had referenced a few times, as part of the amalgamation of information you used for your methodology?

A That's correct.

Q Okay. And so it's safe to say you're familiar with this article?

A Somewhat. I haven't read it in a long time.

Q Okay.

A I read this early on in my process.

Q Would you say that it was important in designing your methodology when you first started working on this case?

A I would say I took it under consideration.

Q Okay. I'd like to go to what has been marked as 270.9, the very bottom of that page.

Do you see a heading that says: "Scope and applicability of the tool"?

A Yeah, I do.

Q Okay. And if you read here, it says: "The scope of the tool is only for assessment of the clinical relevance

of a preclinical research study in terms of the likelihood that therapeutic preclinical findings can be translated into improvement in the management of human diseases and not for assessment of the quality of the study that is how well the study was conducted, although we refer to tools that assess how well the study was conducted.

Did I read that reasonably correctly?

A You did.

Q Okay. And so is it your understanding that the variables within this study were meant for use in assessing the safety of an existing pharmaceutical compound?

MR. PADGETT: Object to form.

THE WITNESS: First of all, I don't think anything in my report talks about the safety of an existing pharmaceutical compound.

BY MS. HUNT:

Q You don't think --

A Number one. I know it doesn't.

Number two, and I'm not quite finished. If you can just take a breath for just one second.

Q Okay.

A So I looked at this article because it's about how well the animal preclinical research tools are translating into the human condition, which is what we're talking about in this case.

Q So I need to unpack, I guess, what you said.

You just testified that you don't think anything in your report talks about the safety of an existing pharmaceutical compound; is that right?

A In humans, yes.

Q In humans. Okay.

A I don't think I mentioned the word "safety" in my report. I'm not sure.

Q So sitting here today, you don't have an opinion on whether Tylenol is safe for use in pregnancy?

MR. PADGETT: Object to form.

THE WITNESS: Oh, I have an opinion on that, but it's not in my report, and the purpose of my report, as I've stated multiple times so far, was to review the rodent literature with respect to the question of whether acetaminophen, given to the rodent equivalent of human gestation, is evidence to support cause, it has any bearing on causality of ASD and ADHD in humans that are exposed to acetaminophen, and whether there are biologically plausible mechanisms.

That was the scope of my report and my systematic review before the rebuttal section.

BY MS. HUNT:

Q So are you planning to come to trial and tell this jury that you believe acetaminophen is safe for use in

pregnancy?

MR. PADGETT: Object to form.

THE WITNESS: It's -- I don't have any plans whatsoever regarding this case beyond this deposition today.

BY MS. HUNT:

Q Okay. Well, Dr. Powell, you -- you may not know this, but under the federal rules, we're entitled to know the full scope of your opinions, so I'm trying to understand.

You're telling me you have an opinion that Tylenol is safe for use in pregnancy, it's just not in the report, right?

A What I'm telling you is that my report and the systematic review largely focused on the rodent literature, and I do have an opinion on the matter you spoke of as a physician, but that was -- that's outside of the scope of my systematic review.

However, I do have an opinion, and I'd be happy to, you know, talk about it if you ask me about it.

MS. HUNT: Okay. I just would say for the record that to the extent that Dr. Powell plans to offer any additional opinions, we would reserve our right to come back and depose him again once we get those reports.

MR. PADGETT: If asked by you or as part of what the defense has put forth in his report as his opinions to be offered at trial?

MS. HUNT: I'm just trying to understand what his opinions are.

So if -- if Dr. Powell is telling me that he has other opinions about the safety of acetaminophen, I'm letting you know that we will depose him on those when and if he offers a report explaining them.

MR. PADGETT: Beyond the scope of his current report?

MS. HUNT: Yeah. Well, he says it's not in his current report, so, okay.

BY MS. HUNT:

Q I'd like to move back to the exhibit, if we could. There's another spot here on the page marked 270.3.

It's about three sections down, it says: "Who is this intended for?"

And underneath that heading, it says: "This tool is intended for all preclinical researchers and clinical researchers considering translation of preclinical findings to first-in-human clinical trials, the funders of such studies, and regulatory agencies that approve first-in-human studies."

Did I read that reasonably correctly?

A You did.

Q Okay. And is it your understanding that the situation we're in now is something related to first-in-human studies or first-in-human clinical trials?

A Not first-in-human, no. But drugs that are used in humans, and it's about the effects on rodents.

And the reason I looked at this article and imported to create my process of systematic review is because it was what I could find that talks about the actual analyzing whether a mouse model finding is applicable to humans.

That's why I felt it was relevant.

Q Okay. Okay.

All right. I'd like to go back to talking a little bit more about multiple comparisons, if we could.

Tell me a little bit about your understanding of the purpose of correcting for multiple comparisons.

A I've explained it in my report, and it's basically -- if you're measuring multiple things and you're analyzing each thing with statistical measures that don't correct for multiple comparisons, that increases the likelihood that you're going to have a false positive finding for the most part. That's a simple explanation.

Q And would a more abbreviated version of that be to say it's to avoid type I errors?

A That's one way of putting it.
Q Okay. What are type II errors?
A The idea that you want to avoid making a false negative.
Q Okay. And in a situation where there might be a threat to human health, a type II error can be a problem also, right?
MR. PADGETT: Object to form.
THE WITNESS: If there were a situation where there might be a threat to human health, then it might be an issue, yes.
BY MS. HUNT:
Q Okay. And if you correct for multiple comparisons, that makes type I errors less likely, right?
A Yes, that's my understanding.
Q Okay. But it can make type II errors more likely?
A Yeah. I don't have enough information to answer that --
Q Okay.
A -- question. Sorry.
Q Can I have 226? All right. Let's take a look at this article. This is the exhibit I've marked as 226.
(Powell Deposition Exhibit 226 marked for identification.)
BY MS. HUNT:

Q And Dr. Powell, the title is: "What is the proper way to apply the multiple comparison test?"

Are you with me?

A Yes.

Q Okay. And I'd like to look at the abstract first.

Okay. So a few lines down within the abstract it says: "In this paper, we discuss how to test multiple hypotheses simultaneously while limiting type I error rate, which is caused by alpha inflation."

A I know I'm interrupting, but I don't see where you are.

Q Oh, okay.

A I would like to.

Q Yeah, take your time. So if you're at the top of the abstract.

A Is it "a problem occurs," is that where you're starting? Or "in this paper."

Q "In this paper."

A Let me find it.

Q Two lines down from "a problem occurs," and I'm sorry, I --

A That's okay. You didn't do anything wrong. I'm just trying to figure this out.

So it's to choose the appropriate test?

Q "Consequently, in an MCT, it is necessary to

control the error rate to an appropriate level. In this paper, we discuss how to test multiple hypotheses simultaneously, while limiting type I error rate, which is caused by alpha inflation. To choose the appropriate test, we must maintain the balance between statistical power and type I error rate."

Do you agree with that?

A Sure, that seems reasonable.

Q "If the test is too conservative, a type I error is not likely to occur. However, concurrently, the test may have insufficient power" -- I think this is a typo -- "resulting in increased probability of type II error occurrence."

Did I read that reasonably correctly?

A I don't believe that has anything to do with multiple comparisons, per se, but it's true enough.

Q So it's your testimony that type II errors don't have a relationship to multiple -- to correcting for multiple comparisons?

A That is not what I said.

Q Okay. Can you explain what you mean?

A Well, I -- having -- looking at this article, that sentence doesn't say the words "multiple comparison test." It just talks generally about which test one is using statistically to evaluate one's data.

Q Okay. But zooming out, when you are talking about correcting for multiple comparisons, you're talking about using a statistical test in order to limit type I errors or spurious findings, right?

A What I'm talking about is -- what I believe they're talking about here is choosing the proper statistical test to begin with.

Q Right.

A Because some are a little bit more lenient and some are a little bit strict.

Q Right.

A That's what I believe they're referring to.

Q We are on the same page.

A Good.

Q Okay. Let's turn to what's been marked as 226.5.

And do you see the section that says: "Bonferroni method"?

A Mm-hmm.

Q Okay. And in the second paragraph of that section, the authors have a discussion about the Bonferroni method where they say: "It has disadvantages as well, since it is unnecessarily conservative with weak statistical power. The adjusted alpha is often smaller than required, particularly if there are many tests and/or the test statistics are positively correlated. Therefore, this

method often fails to detect real differences. If the proposed study requires that type II error should be avoided and possible effects should not be missed, we should not use a Bonferroni correction."

Did I read that reasonably correctly?

A I believe you did.

Q Do you disagree with any of that?

MR. PADGETT: Object to form.

THE WITNESS: I'm not sure I agree with Bonferroni being -- well, hang on. Let me just read the first paragraph so I understand the context real quick.

MS. HUNT: Yeah. Take your time.

THE WITNESS: Thank you.

So, first of all, I want to point out in answer to your question that the first paragraph, first sentence, speaks of clinical trials.

Second of all, I would point out that there's a -- they've made a distinction between using the Bonferroni method as a post hoc test after ANOVA, and I wouldn't necessarily agree that the Bonferroni statistical method is unnecessarily conservative --

MS. HUNT: Okay.

THE WITNESS: -- with weak statistical power.

Now, I would agree that it's unnecessarily

conservative when you have weak statistical power.

I think that -- to take a step back.

None of the articles that I've reviewed, that I recall, reported any sort of power analysis to determine the number of animals that they decided to use.

And so in the specific case of having weak statistical power, I would agree that it's unnecessarily conservative.

MS. HUNT: Okay.

THE WITNESS: Because weak statistical power results in -- in itself a confound for a study.

BY MS. HUNT:

Q Right. And it's important, if you're going to employ a conservative statistical correction, that you have adequate power, right, to find something statistically significant?

A I wouldn't qualify it like you did. I would say it's important to have sufficient statistical power to detect a change that is somehow determined to be meaningful.

Q Okay. Should you also take into account the statistical tools you might use in your analysis?

MR. PADGETT: Object to form.

THE WITNESS: Well, yes. Especially if one's testing multiple, multiple different things within an

experiment.

BY MS. HUNT:

Q Okay. So I know we've talked about this a few times, but Saad 2016, is one of the two papers that you determined were most relevant for purposes of your analysis; is that fair?

A No, that's not correct. As I keep stating, I considered every single result and every single paper regardless of quality, regardless of criticisms, regardless of flaws in the second half my analysis, that's number one.

Number two. With respect to the first part of my analysis, I'm simply listing all the potential flaws and concerns that I have about every single one of those papers.

And then I take a step back in the second part, and I do say, you know, if we were going to -- I mean, I don't eliminate any papers, I just say: Here's a couple of papers that survived that and are without -- essentially without those criticisms, in particular.

And then I considered all the papers' results and all the experiments' results independently of putting them all in a bucket of this paper or that paper, and I drew my conclusions.

Q All right. Let's go to Exhibit 201, which is your report, page 30, paragraph 67. At the very beginning of it.

"Two papers passed criteria for relevance to the

condition of concern and appropriateness of experimental design and statistical analysis."

Did I read that reasonably correctly?

A In the first portion of my analysis, that's what I did, as I've told you. And in the later half of my analysis, which you are dying to ignore, apparently, I -- it discounted all of those potential flaws that are listed, and I took the data at face value and came to the same conclusion.

Q Okay. Dr. Powell, I can assure you I'm not dying to ignore any part of your -- any part of your report.

I'm, in fact, excited to talk about all of it.

So I'm just trying to understand if Saad is one of two papers that you felt, I think in your words, passed criteria for relevance.

A And appropriateness of experimental design and statistical analysis.

Q Okay. So that's correct. That language in your expert report is correct?

A The language is correct, and it does not capture how I did my full analysis of the literature.

Q That's totally fine.

A Thanks for your testimony.

Q Is it your opinion that Saad has been replicated?

A In total?

Q In any part.

A It would take a lot of looking to figure that out, but I can, in part, let me see, where did I go. Let me read that paragraph where I talk about Saad.

I seem to have lost my place.

Q I believe you talk about it at paragraph 67.

A Thank you.

Q On page 30.

A So with respect to open field total activity, open field rearing. Open field -- hang on. Let me see.

Hang on. Yeah, I can't answer that question because I'd have to go back and look at it and look at all the other papers to make sure.

I can't recall, as I sit here today, so I -- I don't remember if it's been replicated or not.

I think that it's part of the inconsistent findings, and so what I would say is here I'm talking about appropriate doses and experimental design and statistical analysis.

Q Okay.

A So I think it passed those criteria, is my understanding, to the best of my recollection, without looking at this paper and having to compare it to every other paper.

Q And the other paper that you mentioned at the

beginning of that paragraph is Baker 2023, correct?

A Yes.

Q And it's a coincidence that that happens to be a paper where Dr. Pearson is the primary investigator?

MR. PADGETT: Object to form.

THE WITNESS: What's your question?

BY MS. HUNT:

Q Is it a coincidence that that happens to be a paper where Dr. Pearson's the primary investigator?

A I don't know what you -- I mean, it's a fact.

Q Okay.

A I don't think it's a coincidence.

Q The fact that he's an expert testifying on behalf of plaintiffs in this litigation didn't have anything to do with the reason that you selected it?

A Not at all.

Q Okay.

A He uses multiple corrections, for example, in his statistical analysis. He uses an excessively large number of animals in his open field task. Among other things.

Q So you think it's a good study?

A It passed the directory of the relevance.

MR. PADGETT: Object to form. Mm-hmm.

THE WITNESS: Experimental design and statistical analysis.

BY MS. HUNT:

Q Are you familiar with Mu Yang, one of the co-authors on Baker 2023?

A I sort of know who she is. I've seen her at meetings and such.

Q She's a behavioral neuroscientist, right?

A Yes.

Q Do you think that it is wise for researchers undertaking behavioral work with animals to have experienced behavioral neuroscientists on their -- on their research teams?

A It certainly doesn't hurt. There's one on all my papers.

Q I'd like to look at what I've marked as Exhibit 213.

(Powell Deposition Exhibit 213 marked for identification.)

BY MS. HUNT:

Q Dr. Powell, are you aware that Dr. Pearson was served with discovery requests in connection with his work on this litigation?

A I have no idea what you're talking about.

Q Okay.

A I don't think -- I mean, I think -- I guess I have seen in a deposition, allusions to e-mail conversations that

I presume may be what you're referring to.

Q Okay. Are you aware that he produced about 2,000 pages of documents as part of his work in this litigation?

A I have no reason to know that or -- no.

Q All right. Do you know that those documents include information about the analyses performed in Baker 2023?

A I don't recall that.

Q Okay.

A In the deposition, but may have.

Q Would it have been useful or interesting for you to know what went on behind the scenes in terms of how that paper was drafted and how the experiments were performed?

MR. PADGETT: Object to form.

THE WITNESS: In -- as a scientist, I review the literature and that's not something that I routinely have access to, and I don't think it's -- I don't know whether it's relevant or not.

BY MS. HUNT:

Q So you wouldn't have been interested to see it either way?

A It would depend on what it contained, of course, but that's not generally an accepted procedure in systematic reviews of the literature as a scientist to go through the e-mail conversations leading up to the publication or drafts

of a paper, so I don't think it's necessary for this type of analysis. And so you must rely on what's in the paper before you in the supplemental information would be my opinion.

Q Okay. All right. Well, I'll represent to you that Exhibit 213 is part of what was produced by Dr. Pearson in this litigation.

Dr. Powell, do you know who John Talpos is?

A I do not.

Q Okay. I'll represent to you that he's the director of neurotoxicology at the National Center for Toxicological Research.

Are you aware of what the NCTR is?

A I understand the concept.

Q Okay. Do you know that it's part of the FDA?

A I was not aware of that.

Q Okay. And if you look about halfway down this page, where it says: "March 20th, 2023."

A Which page? The first page?

Q First page.

A All right. Thank you.

Q At 1705, Talpos, John. And then it has an e-mail address.

Does it appear to you that he's an FDA employee?

A It appears that he has an FDA in Health and Human

Services, a governmental e-mail address. I don't know if he's employed there or not.

Q Okay. Let's go all the way to the back of this exhibit, the page marked 213.3.

Does this appear to you to be an e-mail from Dr. Pearson to Dr. Talpos?

A Dr. Pearson to Dr. Talpos. I'm going to have to look at the previous page.

It looks like it's from Dr. Pearson to John Talpos.

Q Okay. And it says: "Hi John, this is that mouse paper. Do you see effects in their behavioral and histopath results?"

Did I read that correctly?

A You did.

Q Okay. And I took the liberty of pulling up that URL, and I've marked that as Exhibit 221.

(Powell Deposition Exhibit 221 marked for identification.)

BY MS. HUNT:

Q And Dr. Powell, does this appear to you to be the Saad 2016 paper?

A It doesn't look like my copy, but it may be. Okay. I'm not -- let me double-check, because I'm not --

Q Take your time.

A I just want to make sure, because I have it printed out a different way and that doesn't mean it's not the same. Saad 20 --

Q Saad 2016.

A Thank you. Ah, yes, same title.

Yes. This looks more familiar to me. I'll just go off this, if you don't mind.

Q Okay. That is no problem.

And moving back to Exhibit 213.

I'd like to look at the page marked 213.2. About halfway down the page, there's an e-mail from John Talpos on March 20th, 2023, at 2:43 p.m.

Just let me know when you're there.

A I'm there.

Q Okay.

A At 2:43 p.m?

Q Yes.

A Where it says -- yeah.

Q And does this appear to be an e-mail from John Talpos?

MR. PADGETT: Object to form.

THE WITNESS: It does.

BY MS. HUNT:

Q Okay. And I'm going to read what it says.

And I guess I should ask, does this appear to be a

reply to Dr. Pearson's e-mail, which includes the Saad study?

A Given the way this is put together, I'm not sure I could read it, but it could be.

Q Okay. All right. Well, I'm going to read Dr. Talpos' e-mail.

He says: "This paper is really weak. I admire them for correcting for multiple comparisons. I think we should do more of this in behavior. However, they are way underpowered for their requirement for significance. I have a feeling this group does not publish much behavioral work."

Did I read that reasonably correctly?

A You did.

Q Do you agree that the Saad authors were underpowered for their requirement for significance?

A Let me take a quick look.

Q Take your time.

A What I'm trying to do is figure out what the end use in their experiments was, and if I remember correctly, they used two males -- what I just read was two males and two females from each litter, and now I'm trying to go through the paper, and I remember doing this previously, because when I initially read this paper, I thought, wow, that's an incredibly low end, four total.

But then you have to dig to figure out how many

litters there were, and to find out what their end was for each experiment.

So I'm going to -- that's what's taking long and it's because it's not readily apparent, but I may have it in a table, but let me just -- let me see if I have it in a table in my report. It's possible.

A table. And that might be a faster way to do it.

Otherwise, I'll have to read the whole article and recapitulate some work that I've already done.

Let's see. Saad 2016. Okay. There it is.

Ooh, I don't have the in in there either, okay. So I'm trying to figure out how many litters there are.

Ah, here it is.

So for the behavioral experiments, the in was 16 per group, which I do not believe is -- I mean, it may be underpowered, but I can't do -- I have not done a power analysis on this specifically, but an in of 16 is within the realm of acceptability per Silverman, per Dr. Rochelle Tyl, and others in the field.

So I don't have issue with that being underpowered.

I believe it's quite likely that what Dr. --

Q Talpos.

A -- Talpos is referring to is Figure 3, which I basically don't think is -- shows much of anything and is

definitely underpowered, in my opinion.

However, I was focusing more on the behavioral findings.

Q The --

A I see that it has no findings, and the thing, I would agree that for that particular experiment, it's underpowered.

Q And do you acknowledge that anywhere in your expert report?

A I don't know, that's a good question.

Q Do you agree with Dr. Talpos that the Saad paper is, I think he called it, really weak?

A With respect to --

MR. PADGETT: Object to form.

THE WITNESS: With respect to the fact that they met multiple of my criteria for the behavioral studies, I don't agree.

But in terms of the initial staining, which I don't think is particularly that revealing or relevant, I think it's underpowered, and I would say that's a reasonable characteristic of Figure 3, but not of the behavioral outcome measure.

BY MS. HUNT:

Q Okay. And he says: "I have a feeling this group does not publish much behavioral work."

Did you look into the backgrounds of any of the people who worked on the Saad study?

A I did not. And I don't know the basis of Talpos, what this guy's -- who's being -- communicating with Brandon Pearson's judgment on that was.

The open field is -- is a task where you literally put the mice in a box and see what they do and how much they move, and it's either recorded by a video tracking instrument or beam brakes, or something like that, so it's a behavioral task, it's probably the most straightforward and I -- it would be something that virtually any laboratory who can read the literature can do, anything related to neuroscience.

So I disagree with the idea that to put an animal into an open field and measure beam breaks and whether they're the center of the periphery requires a behavioral expert like Dr. My Yang, and I think she -- well, I don't know, I shouldn't say.

Q Okay. But in your own work, you testified that you liked to have a behavioral neuroscientist on all your papers involving behavior, or did I hear that wrong?

A Yeah. I think you are misquoting me.

I think I said I think it's a good idea to have someone and all my papers have one, myself. So --

Q Got it.

A -- there you have it.
Q And I think we talked about this a little bit earlier, but is it -- let me back up.
It sounds like you read the deposition of Dr. Pearson?
A At one point, yes.
Q Okay. And in his deposition, do you recall if Dr. Pearson talked about how important the epidemiology is to his work as a neurotoxicologist?
A The human --
MR. PADGETT: Object to form.
THE WITNESS: Yes.
MR. PADGETT: Same objection.
THE WITNESS: I don't, and I'm not sure what -- I'm not sure what you're really asking about.
Do I remember the fact that he thinks it's important to understand epi as a toxicologist?
BY MS. HUNT:
Q Yeah, in other words --
A I don't disagree with that. I have to understand the epi in my work.
Q Okay. Would you say that --
A As a non-neurotoxicology Ph.D.
Q Okay. So more broadly, in behavioral neuroscience, it's important to understand the epi; is that

fair?

A Okay. Well, if you're going to do experiments, is it important to understand the epi.

You can do an experiment on a compound and look at its effects in mice and rodents and be completely agnostic of the epidemiological literature, that is possible to do.

In many cases, there are studies where compounds are given to animals, where there's little or no epi, as far as I'm aware.

So I don't know what you mean by "important," so I think it's kind of an ambiguous question.

Q Well, do you think these neurotoxicologists doing preclinical research are taking epidemiology into account when they decide what compounds to expose rodents to?

MR. PADGETT: Object to form.

THE WITNESS: Oh, just -- I think that they sometimes think about that.

Other times they're agnostic to the human epi and test compounds that are in the environment. From time to time. Without -- with the absence of any human epi data, but I don't -- I can't cite studies or anything off the top of my head right now.

I would say that as a person who studies genetic animal models, I use the human genetics data to inform the choice of some of my animal models, not all

of them though, there are cases where I've -- there's zero human connection to any disease.

And I've looked at the effects of those genes and how they affect synaptic transmission, plasticity and behavior, so, you know, it's very a context opinion, I would say.

BY MS. HUNT:

Q Okay. But in the context of neurotoxicology, there would be no reason to dose these animals with a compound if you didn't think that compound was having an effect on human health, right?

MR. PADGETT: Object to form.

THE WITNESS: I think that there are toxicology studies that give -- that I believe, I can't say with 100 percent certainty, but I'm pretty sure there are studies where they give rodents chemicals that haven't shown any effect in humans in epidemiologic studies, but I can't say that's 100 percent true.

(Powell Deposition Exhibit 225 marked for identification.)

BY MS. HUNT:

Q Okay. I'd like to show you what I've marked as Exhibit 225.

And, Dr. Powell, just looking at the first page,

it says at the top: "National Center for Toxicological Research;" is that right?

A Right.

Q And beneath that it says: "Science Advisory Board Meeting, May 19th, 2022."

Did I read all that correctly?

A Yes.

Q And so let's take a look at this document, and I will represent to you that this is a transcript of a science advisory board meeting. And I'd like to turn to what's been marked as 225.28.

And do you see the bolded text there that says: "Agenda Item, Division of Neurotoxicology."

Are you with me?

A Yes, I do. I see that.

Q Okay. And then it says right beneath that from Dr. Talpos.

"Thank you for your time. I am John Talpos, the Director of the Division of Neurotoxicology, and I am going to provide an update on activities within the division and we would love your input on current, as well as our future activities, because a lot of the current work I'm presenting today is still very much in progress."

Did I read all of that reasonably correctly?

A Sure. Yes.

Q Okay. All right.

Now, let's go -- so does it appear to you that this is testimony from Dr. Talpos?

A It is not.

Q It's not Dr. Talpos?

A It's not -- it is Dr. Talpos.

Q Okay.

A But it's not testimony, as I define it.

Q Okay.

A As I understand it's defined generally.

Q Okay.

A When I'm at a deposition under oath testifying as if I were in front of a jury and a judge, this is not testimony of that sort --

Q Touche.

A -- in my understanding.

No, it's not a dig. It's just a explanation.

Q All right. Let's go to what has been marked as 225.38, and I'm just going to start right at the top, and I'll represent to you that this is still Dr. Talpos talking.

He says: "Moving to future projects, I want to talk about a project that we're putting together to look at the developmental neurotoxicity of acetaminophen in a vitro setting. Our ongoing efforts to establish the regulatory impact of damage to barriers of the CNS and our plans to

develop the mini swine as a model for developmental neurotoxicity testing and other studies."

Did I read that correctly?

A You did. Barriers to -- of the CNS damage, yes.

Q Okay. So Dr. Talpos continues on here, and he says: "So there's a growing concern about the potential toxicity of in utero exposure to acetaminophen as highlighted by this 2021 consensus statement. The concerns over APAP" -- and you understand that to be acetaminophen, right, Dr. Powell?

A Yes, I do.

Q -- "are being driven by a series of high-quality epidemiological studies."

And I think we already discussed you disagree with Dr. Talpos about the quality of the epidemiological studies, right?

MR. PADGETT: Object to form.

THE WITNESS: Well, I don't know which studies he's referring to. He talks about a, quote-unquote, series of high-quality epidemiological studies.

I didn't never once said that there aren't any high quality or decent quality epidemiologic studies.

I had concerns about several of the studies

in terms of their quality and their use and utility with respect to the question in this case, whether acetaminophen during human gestation leads to an increased risk or causes an increased risk of autism spectrum disorders or attention deficit hyperactivity disorders.

BY MS. HUNT:

Q Which epidemiological studies in this case would you call high quality?

A I don't have enough information to answer that question because I read these a long time ago, and I don't have them all memorized.

Q Okay. So there aren't any that stick out in your mind as, wow, that was a pretty good study?

A Well, I would say that the studies, to the -- losing my words, call the ambulance. No.

With respect to the question of causality in humans, or even association in humans of acetaminophen to ASD and ADHD diagnoses, I would consider that the other studies that don't use that as their endpoint are of lower quality to answer that question for that very reason alone, but that's my opinion.

Q Okay. So is it your opinion that the studies that did use a formal clinical diagnosis of ASD or ADHD are high quality?

A I would say that's too vague a term that I can't define, and I don't know what he means so I can't really answer that question. I'm sorry.

Q All right. We will continue.

Dr. Talpos says: "A recent meta-analysis of these studies showed a 20 to 30 percent increased risk of autism spectrum disorder and ADHD in boys exposed to acetaminophen in utero. The risk isn't" -- and I think it's supposed to say "limited to boys alone, however, it is notably higher in boys than in girls."

And I want to stop there for a moment.

Dr. Powell, are you familiar with the meta-analysis that Dr. Talpos is referencing here?

MR. PADGETT: Object to form.

THE WITNESS: No one could possibly be familiar with the meta-analysis because he doesn't say which one it is. So I don't think anyone could possibly know what meta-analysis this is.

BY MS. HUNT:

Q Okay. And would you agree with me that sex-specific differences in general are a hallmark of neurodevelopmental disorders?

MR. PADGETT: Object to form.

THE WITNESS: I would say that autism spectrum disorder is more prevalent in males than

females of a ratio of three or four to one, favoring boys getting the diagnosis.

And in ADHD, I think it's on the order of 1.9, give or take, to 1, males over females.

BY MS. HUNT:

Q Okay. And boys and girls with neurodevelopmental disorders can also present differently; is that right?

MR. PADGETT: Object to form.

THE WITNESS: Any patient with an autism spectrum disorder or ADHD can have differences in their presentation as long as they meet the DSM-V criteria for the disorder.

And especially that they've ruled out that that it's caused by other disorders, like anxiety disorders and other neuropsychiatric or neurodevelopmental disorders, depression and all that. That's in the DSM-V.

BY MS. HUNT:

Q Are there commonalities in the literature seen in the differences between boys and girls with ASD or ADHD?

A Well --

MR. PADGETT: Object to form.

THE WITNESS: My understanding in the ADHD world is that it's a little more likely in a girl that they're going to have ADD, attention deficit disorder

without hyperactivity, and in boys a little more higher incidence of ADHD, but that's really the only -- that's only at a conceptual level, and I'm not prepared to really speak more to that in detail.

BY MS. HUNT:

Q When -- when you're --

A Also I would add -- sorry. That in the case of ASD, the male to female ratio has not been fully explained, and there are many people who feel like there are cultural reasons why girls are less likely be diagnosed with autism spectrum disorder than boys.

Third, I would say that if you have a known cause like a rare de novo mutation, many of those do not have sex differences in their incidence.

Q But many of them do, right?

A I wouldn't say many.

MR. PADGETT: Object to form.

THE WITNESS: If you're asking me about genetic causes of autism, I would not agree with the statement that many rare de novo genetic mutations that are highly penetrant for autism spectrum disorder, I wouldn't say that many of them are more prevalent in boys than girls.

Some of them have been shown to be, but that's not -- I think that's the exception in my

understanding of that literature rather than the norm.
BY MS. HUNT:
Q All right. Let's continue on with this document.
So he goes on to say: "And I'd also like to draw your attention to the cumulative sample size in these studies. They're really very big and it's an impressive dataset highlighting this potential concern."
Did I read that correctly?
A You did.
Q And do you agree that the cumulative sample size in the epidemiologic body of literature is impressive and very big?
MR. PADGETT: Object to form.
THE WITNESS: Well, I would say that sample size is virtually irrelevant if you consider the fact that most, if not -- most of the studies that I read in the epidemiologic literature had -- many of them had large sample sizes and they did not control for the most important cause, known cause of autism, which is genetics.
BY MS. HUNT:
Q Okay. So is the answer to that yes or no?
MR. PADGETT: Object to form.
THE WITNESS: I answered your question, and if you want to read it back, that's my answer to the

question.
BY MS. HUNT:
Q Okay. Do you agree that the cumulative sample size in the epidemiological literature is impressive and very big?
MR. PADGETT: Object to form.
THE WITNESS: I would agree that it's very big.
BY MS. HUNT:
Q Okay. But --
A I think -- and as we've spoken about, I think the papers have serious lack of control for important elephant in the room, majority of autism, vast majority of autism cause is genetics.
Q Okay. And so you disagree with the director of neurotoxicology for the National Center for Toxicological Research within the FDA in terms of the impressiveness of the dataset --
MR. PADGETT: Object to form.
BY MS. HUNT:
Q -- in the epi?
A Impressiveness of the dataset?
Q Yeah.
A I don't disagree with him about the impressiveness of the dataset in terms of its size.

Q Okay.

A But to the extent that most of these studies did not even concern themselves with the most important confound, which is that 75 to 80 or more percent of ADHD and ASD are caused by genetic changes.

Q Dr. Powell, if all of those ASD cases are genetic, would that same -- wouldn't that same gene also have to cause the mother to take more acetaminophen in order to be a confounder in the epi?

MR. PADGETT: Object to form.

THE WITNESS: Well, I think you're asking a very complex question, I'll try to address it.

There are many reasons why a person may or may not take more or less acetaminophen during pregnancy.

There are studies that relate certain genetic tendencies or risks with a tendency to take more acetaminophen in general, and I think during pregnancy, but I won't put my life on that, and so that is one possible explanation.

MR. PADGETT: We've been going for an hour and 10, so whenever you're ready for a break.

MS. HUNT: Okay. As soon as I'm done with this document, we'll take a break.

BY MS. HUNT:

Q Do you know of a gene that's been discovered that encourages women to take more Tylenol during pregnancy?

A A single gene, no.

Q Okay.

A I just -- I feel remiss not pointing out that your famous and respected Dr. Talpos, is it?

Q Mm-hmm.

A Speaks, in two sentences below, where we just -- we just quoted that "our lack of knowledge about the mechanism behind potential, potential APAP mediated nerve toxicity makes it a little bit difficult to design assessments."

Q Oh, you got ahead of me, but don't worry, I was -- I was getting there, so we can talk about that now.

And you're right. He says: "Within the division, we're starting to research APAP-related neurotoxicity with in vivo models. However, our lack of knowledge about the mechanism behind potential APAP mediated neurotoxicity makes it a little bit difficult to assign assessments, and there are multiple mechanisms by which APAP may cause neurotoxicity, as you can see here. However, one potential mechanism popped out as lending itself to evaluation in an in vitro setting, and that's CYP2E1 mediated metabolism, and that's a project that's being led by Dr. Shuliang Liu."

Did I read that reasonably correctly?

A Yes. Especially the part that says "may and potential."

Q Right. That's -- those are the parts you like, right?

A And project -- no. And there's a project that's being done to test that potential mechanism whereby APAP may cause neurotoxicity.

So, you know, you definitely read it right, but I just want to make sure it's clear what it says for the jury's sake.

Q All right.

A And what it doesn't say.

Q All right. So he continues on to say: "CYP2E1" -- which, Dr. Powell, we talked a little bit about CYP2E1 earlier, right?

A Yes.

Q "CYP2E1, a lot of you probably know a lot about it, is highly expressed in the liver. APAP metabolized by CYP2E1 will eventually deplete levels of glutathione resulting in free radical formation and hepatotoxicity."

Did I read that correctly?

A Yes. And I'll just note that doesn't talk about dose, duration, et cetera. And I'll reiterate what I've answered before was I have never seen any literature saying

that glutathione is depleted in the fetal brain, in humans, rice or rats.

Q He continues on to say: "While CYP2E1 is expressed in neurons in the human brain, it is at lower levels than in the liver, but it's very much still there."

Do you disagree with Dr. Talpos about that?

MR. PADGETT: Object to form.

THE WITNESS: Thank you. It depends. Sorry.

It depends on whether -- what he means by the word "expressed" on neurons, and he doesn't state that.

I would agree that there are detectable MRNAs that are very low compared to the liver and the human brain, I think, or maybe it's mouse -- I can't remember if it's human or mouse, to be perfectly honest with you, and the protein levels are, if at all detectable, barely detectable, and I've seen no repetitive, qualitative -- quantitative western blots done on the fetal brain of rodents or humans that I can recall that demonstrates, in a statistical manner, with multiple iterations of testing, you know, where you test multiple brains and have a high in and you measure western blots and you quantify them and you relate that to some known control, protein expression.

So I think this sentence is -- says what it says but it's ambiguous, and it's impossible to know

exactly what he means, and I think that's a very important point in this case.

BY MS. HUNT:

Q He continues on: "This raises the question if CYP2E1 mediated toxicity could occur at the brain. If so, this is potentially really problematic as alcohol" -- you're going to have to help me with this word, Dr. Powell.

A Halogenated anesthetics.

Q "Halogenated anesthetics, and even a metabolite of caffeine are all metabolized by CYP2E1. So there is very real potential to push this system too far."

Did I read that correctly?

A You read what that says.

Q Okay.

A And I would say that --

Q Sorry. Go ahead.

A -- it needs to be clarified what it does and doesn't mean because the majority of alcohol, as I understand it, halogenated anesthetics, and even metabolites of caffeine, are metabolized in the liver and not the brain, as I understand it from my medical training and my limited knowledge of this subject in terms of metabolism of alcohol, halogenated anesthetics and metabolites of caffeine.

Q Okay. And then he --

A So I would also state that --

Q Oh, sorry. Go ahead.

A So I would also state that -- so there's a real potential to push this system too far is -- it's not clear what he means, which organ he's talking about, what doses he's talking about, what duration he's talking about.

And so, I mean, it says what it says, and it's difficult to ascertain what it means specifically.

Q And then he continues on to say: "And, of course, the developing brain is very vulnerable to all types of different abnormal energetic demands."

Do you agree with that?

A Well, so --

MR. PADGETT: Object to form.

THE WITNESS: -- the brain makes up about 5 percent ever the weight of the human body and it consumes about 20 percent of the energy in the human body, and it relies largely on glycolysis.

So I think that's a reasonable explanation of what he's trying to say in a scientific term.

BY MS. HUNT:

Q And while we're talking about organ systems -- and this is the last set of things I'll ask you before we take a break, but when we're thinking about different organ systems, like, for example, the brain versus the liver, isn't one of the things that distinguishes the brain as an

organ the fact that it can't regenerate?

A That was classically the thought and, generally speaking, that's true. However, for the accuracy of my answer, I have to say that there are new neurons born in the intake gyrus of the hippocampus throughout life and that there're continually newborn neurons migrating to replace olfactory neurons of the brain.

But, generally speaking, the neurons in the brain don't regenerate.

Q Okay.

A Generally speaking.

Q But the liver can regenerate, right?

A Yes.

Q Okay.

MS. HUNT: I'm good to take a break now, Bill.

MR. PADGETT: 10 minutes.

THE VIDEOGRAPHER: Off record, 2:02 p.m.

(Off the record at 2:02 p.m.)

THE VIDEOGRAPHER: On record, 2:20 p.m.

BY MS. HUNT:

Q Okay. Dr. Powell, I'd like to go back to your expert report, which has been marked as Exhibit 201. And I'd like to go to the bottom of page 24, we'll start there.

And I guess I should preface this by backing up

and saying this section of your report, as I understand it, is about translationally relevant dosing in preclinical studies; is that fair, Dr. Powell?

A Yes. It's about -- it's musings on the -- what the doses ought to be and what models, I think.

Q Okay. And so you say at the bottom, the very bottom of page 24, you say: "For example, extensive human studies demonstrate that acetaminophen does not typically result in toxicity at maximum labeled doses of up to 4,000 milligrams per day in adults. While potential hepatotoxicity in humans may occur at doses above the maximum label dose of 57 mgs per kg per day at approximately 150 to 200 mgs per kg per day and following acute overdose."

Other than the citations, the strings of citations, have I read that reasonably correctly?

A Yes.

Q Okay. In your research and as a clinician, how do you determine if hepatotoxicity is occurring in a human subject?

A You need to define hepatotoxicity. If you mean some minimal damage to some subset of cells in the liver, we could look at spillage, literally spilling of AST and ALT into the bloodstream.

If you mean through hepatotoxicity to the point that there's decreased function of the liver then we

typically look at coagulation factor, levels of albumin and development of protein.

Q Okay. And --

A Oh, sorry. And we look at bilirubin and other functions.

Q Yeah, no, you're fine.

And in a human, is it possible to be experiencing signs of liver damage and not know it?

MR. PADGETT: Object to form.

THE WITNESS: That's a little bit too broad and ambiguous for me to answer.

What I would say is your -- it depends on the extent of the liver damage and whether you have functional liver damage that causes symptoms or not, and so you have a range of hepatotoxicity, and I don't know where you're talking about.

Certainly, you can have spillage of AST and ALT in the bloodstream without knowing it.

BY MS. HUNT:

Q Okay. And you cite in your report a series of studies in this section.

Do you know if any of the studies that you cited in this section are double blind randomized control trials?

A I have no idea. I don't recall.

Q Okay.

A I just know what they taught us in medical school that we don't want to give more than -- I mean not just, but I know that we don't want to give more than the maximum amount per day, particularly if there are other comorbidities.

Q I'd like to look at what's been marked as Exhibit 254.

(Powell Deposition Exhibit 254 marked for identification.)

BY MS. HUNT:

Q And Dr. Powell, would you agree with me this appears to be a randomized-controlled trial related to ALT elevations in healthy adults?

A I see that's all represented in the title, yes.

Q Right. It says: "Aminotransferase Elevations in Healthy Adults Receiving 4 Grams of Acetaminophen Daily."

Right?

A That's what it says.

Q And 4 grams is the recommended daily dose that you talked about in your expert report, right?

MR. PADGETT: Object to form.

THE WITNESS: It's the maximum human amount of acetaminophen that one is -- what one could take and be following the label, Extra Strength Tylenol in humans, yes.

BY MS. HUNT:

Q Okay. And if we look on that first page under: "Results," a few lines down, do you see where it says -- the sentence starts: "Compared with placebo."

"Compared with placebo, treatment with acetaminophen was associated with a markedly higher median maximum ALT. Trough acetaminophen concentrations did not exceed therapeutic limits in any participant and after active treatment was discontinued, often decreased to undetectable levels before ALT elevations resolved."

Did I read that reasonably correctly?

A I believe you read the sentence correctly, and we're speaking about minimal cellular damage.

Q Okay.

A And they talk about ALT elevations of this magnitude that are recoverable.

Q Okay. And when you looked at the animal literature, did you consider it a weakness of the study if the animals showed signs of hepatotoxicity like increased ALTs?

A I didn't really comment on that. If the dose was rational or relevant, as far as I remember.

What I can tell you is that a cutoff of 200 milligrams per kilogram per day is, as I spoke about before, a very conservative in terms of the recommended

single human dosage, and it's even with allometric scaling or any other method in mice.

Q Okay. Do you think it's unreasonable for the scientists who were studying neurotoxicity of acetaminophen to use allometric scaling in their experiments?

MR. PADGETT: Object to form.

THE WITNESS: I would say that insofar as -- I'm sorry. What did you ask me, is it what?

BY MS. HUNT:

Q Is it unreasonable?

A Unreasonable.

MR. PADGETT: Same objection.

THE WITNESS: The truth is, I went into this fairly agnostic, read the literature on doses and, you know, I think in -- in -- in a situation where we know all about the peak doses and the area under the curve and toxicity in a drug that's often used in humans, I believe that the allometric scaling, as -- in the document referenced by the expert reports that I read, is intended for first-in-human use, and was not intended for going back and forth between animals to humans.

At the end of the day, though, my cutoff is a higher dose than liver toxic doses in mice and higher than -- or liver toxic meaning these minor changes in

AST or ALT, and higher than what the allometric scaling comes.

So I put in a safety factor on my dose cutoff level of 200 milligrams per kilograms in both rats and mice.

BY MS. HUNT:

Q Why did you choose to use a single dosing cutoff for all rodents?

A Because that is how humans take it, one dose at a time, if they're following the label. And then they wait an appropriate period of time before they take another dose.

And --

Q Oh --

A That's what I used.

Q I'm sorry. I think we're -- I think we're -- I think we're having a miscommunication.

How did you decide that you would use the same number in terms of a dose, 200 mgs per kg, right?

How did you decide to use the same numbers for rats and for mice?

A Oh, again, these were conservative estimates and they're higher than allometric scaling.

Q Okay.

A And so I was being as lenient and conservative as I could because I wanted to know what -- if there was

really -- what was there in the literature that, you know, might lead one to conclude or support causality in humans, if anything, or a plausible biologic mechanism.

Q Are you aware that the majority of the in vivo experiments on acetaminophen's developmental neurotoxicity are in rats?

A I didn't calculate the ratio of rats to mice.

Q Okay.

A No.

Q But you'd agree with me, in general, that it's pretty important to get the dose analysis right in examining this body of literature?

MR. PADGETT: Object to form.

THE WITNESS: I would say that it's important not to exceed a dose level of -- that pushes things into levels that don't correspond to human dosing.

BY MS. HUNT:

Q Okay.

A And my cutoff is higher than that.

Q And when you came to that number of 200 mgs per kgs, were you looking at data on hepatotoxicity in order to come to that number?

A I would say that I looked at multiple things, multiple dosings, multiple sources, to kind of come to a gestalt, because remember, this was before anything -- any

other experts or anything else.

So, you know, I looked in the literature to try to be as conservative as possible to come up with a dosing regimen, and so I looked at liver toxicity in mice and I looked at allometric scaling and certainly dismissed the idea of a safety factor of tenfold in the conversion from humans back to mice because we're not in that sort of situation.

And then, you know, I settled on 200 milligrams per kilogram because it was generous in rats and it was generous in mice, period.

Q Okay. I'd like to go back to your expert report for a moment. So on page 25, again, this is in that top paragraph.

You say: "Similarly, going back decades, the hepatotoxicity of acetaminophen in rodents has been documented in dozens of studies employing a wide variety of experimental conditions that demonstrate liver toxicity after a single day exposure to acetaminophen at doses ranging from 500 to a 1,000 mgs per kg and higher in rats, and from 150 mgs per kg and higher in mice, with mice clearly tracking human toxicity response dose wise."

Did I read that correctly?

A I believe you did.

Q Okay. And is it safe to say, based on that

language, that rats and mice have different vulnerabilities to acetaminophen?

MR. PADGETT: Object to form.

THE WITNESS: It's safe to say that rats and mice have different vulnerabilities to hepatotoxicity than mice, and that's very well documented in the literature that I'm aware of, and that's -- well, that's all I have to say.

BY MS. HUNT:

Q And I realize this might be a silly question, but rats and mice are entirely different species, right?

A They are.

MR. PADGETT: Object to form.

THE WITNESS: They're a different species.

BY MS. HUNT:

Q And they're different sizes, right?

MR. PADGETT: Object to form.

THE WITNESS: Mice and rats, on average, are different sizes, correct.

BY MS. HUNT:

Q Okay. And there's other differences between them, right, in terms of how they metabolize acetaminophen, for example?

A What's your question? I'm sorry.

Q Is it your understanding that rats and mice

metabolize acetaminophen in different manners?

A Yes.

Q Okay. And so despite the fact that there are different species, they are different sizes and they metabolize the drug differently, your opinion is still that there should be a single dose that's appropriate for both?

MR. PADGETT: Object to form.

THE WITNESS: I believe that I could have been much more stringent in my dosing criteria.

However, I was agnostic to what people were going to say about what the most appropriate doses were. There were many studies that had clearly higher than appropriate doses. And studies that were on the border line.

And so what I did was I added a safety factor to be as conservative as possible, which is also why I did my best in my initial analysis to include all the studies.

And then when I rebutted the expert witnesses on -- excuse me, for the plaintiffs, I looked at mostly the papers that they cited and noted that our dosing cutoffs were, in many ways, very similar.

We can look at -- if you'd like, we can look at Dr. Pearson's deposition and what levels of dosing he used for some of the studies to virtually eliminate

the potential consideration.

So I was being conservative to try and give the literature the widest benefit of the doubt.

BY MS. HUNT:

Q So are you saying that the plaintiffs' expert used -- experts used a single dose number as a cutoff for both rats and mice?

A Oh, I don't think I said that. I think what I said was their dosing regimens that Dr. Pearson included in his report and Dr. Cabrera included in his report that I believe are higher than the typical single dose in humans and memory -- and I don't remember exactly what the doses were, the cutoffs for Dr. Pearson to eliminate the studies that he eliminated, but we can look at that if you'd like.

Q Did you notice, in looking at the literature, that the studies involving rats typically involved a higher dose than the studies involving mice?

A It depends on which studies you're talking about. If you're talking about hepatotoxic in liver literature, I don't recall.

And if you're talking about the other, I've already said I don't remember whether there were more rats than mice, so I don't recall.

Q But sitting here today, you can't recall either way whether the researchers studying acetaminophen's

developmental neurotoxicity in rats used higher doses than the researchers studying acetaminophen's developmental neurotoxicity in mice?

A Let's see. I'll just go through some rat studies.

50 milligrams per kilogram. Rat study, 35 milligrams per kilogram. Rat study, 50 milligrams per kilogram. Rat study, 51.97 milligrams per kilogram.

Now let's look at mice. Mice, 150 milligrams per kilogram. Mice, 150 milligrams per kilogram. Mice, 103.9 milligrams per kilogram. Mice, 150 milligrams per kilogram.

And then there's -- let's see. And then there's some mouse studies that give 30 milligrams per kilogram or 30 milligrams per kilogram four hours apart.

So I didn't -- with that particular table, where I looked at people who have -- the studies that passed the hyperactivity or measures thereof, I didn't -- don't see a trend that you're speaking of.

Q Okay.

A If we look at repetitive restrictive behaviors. Rat, 5 milligrams per kilogram and 15 milligrams per kilogram in the drinking water.

There's a rat with 350 milligrams per kilogram. There's a rat -- it may be the same one, so it's the same one with 5 and 15 milligram per kilogram.

Q And are those --

A So there's a lot of variation in the doses used, and I believe that, you know, even using allometric scaling, the individual maximum dose in humans using rat allometric scaling gives you a number on the order of 90 or so milligrams per kilogram, as equivalent to a single human maximum dose of a thousand milligrams.

Not the regular strength Tylenol, which is 650 grams per dose --

Q Dr. Powell --

A Which would be even a lower number.

Q I'm so sorry to interrupt you, but if you could give me a page number.

A Oh, I'm sorry. I'm looking at a couple of pages --

Q I'm just trying to track --

A 76, 77 --

Q -- what's you're doing here.

A 76, 77, 72. Those are the ones that I've gone through so far.

And there are rat studies that use 350 milligrams per kilogram.

I think when there were high doses that were intended to cause liver toxicity, which typically aren't presented in my table, then those are completely eliminated,

so I didn't look at those for a pattern.

Q Okay.

A And all those studies that I rejected for too high a dose correspond quite well, I think, for the most part, with about four or five exceptions with plaintiff experts.

Q Okay. So I'd like to give you what's been marked as Exhibit 257. I think you'll recognize this.

(Powell Deposition Exhibit 257 marked for identification.)

BY MS. HUNT:

Q This is Dr. Pearson's expert report, and I'd like to look at what's been marked as 257.83.

And, Ray, can we pull up another page right next to this?

TRIAL TECHNICIAN: Sure.

BY MS. HUNT:

Q I'd like to pull up right next to it, 257.100.

And, Dr. Powell, I'll represent to you that on the screen in front of you, we've got a chart that shows rat studies involving developmental neurotoxicity.

And on the right-hand side, we have mouse studies. So I guess if we could revisit -- first of all, would you agree with me that there are more rat studies than there are mouse studies on acetaminophen's developmental neurotoxicity?

MR. PADGETT: Object to form.
THE WITNESS: I would say of these papers that are listed, yes.
BY MS. HUNT:
Q Okay. And will you agree with me that several of these studies incorporate multiple dosing regimens; is that fair?
A Two or three different doses, yes.
Q Yes. Okay.
And looking at --
A Oh, were we talking about rats or both, mice and both?
Q Both. You can look at the screen in front of you.
A I got it. Thank you, though.
In the case of mice they used, at most, two doses in this list. Not including zero, of course.
Q Okay. And you're telling this jury that you don't see a trend in higher dose ranges in the rat studies as compared to the mouse studies?
MR. PADGETT: Object to form.
THE WITNESS: I would say that of these studies that have been included in these tables, the maximum mouse dose that is used is 150 milligrams per kilograms per day, and the maximum dose used in rats is as high as 500 milligrams per kilogram, though I think

that's too high, and the majority of the others don't go above 350 milligrams per kilogram.

There's only two that do at that level.

BY MS. HUNT:

Q So can we agree that, in general, many of the rat studies use a higher dosing regimen than the mouse studies?

MR. PADGETT: Object to form.

THE WITNESS: We can agree that four rat studies do.

MS. HUNT: Okay.

THE WITNESS: In these lists, which are selected after eliminating studies with higher -- with doses that Dr. Pearson deems too high, I think.

MS. HUNT: Right.

THE WITNESS: If I'm not mistaken.

BY MS. HUNT:

Q And, okay. And so it sounds like we agree that mice and rats have different vulnerabilities to acetaminophen, right?

MR. PADGETT: Object to form.

THE WITNESS: With respect to liver toxicity, I believe that's well-known.

MS. HUNT: Okay.

THE WITNESS: With respect to any other form of toxicity, I don't believe that's been demonstrated

for the brain, and I don't know about other organs.

BY MS. HUNT:

Q Okay. And it's still your opinion that allometric scaling is inappropriate in this case?

A Well, I think it's --

MR. PADGETT: Object to form.

THE WITNESS: I would say that I don't think allometric scaling with a 10X safety factor in humans would be appropriate to use to go down to mice or rats.

And I think that it's important to think about what the maximum concentration is after some of these doses in mice and rats and ensure that they don't go higher than 132 micromolar, or micromols per liter, which is within the range of what happens after you get a peak dose, or Cmax, as it were, when you give to mice.

And that's according to this particular document I'm looking at.

MS. HUNT: Okay.

THE WITNESS: Yeah. And I'll just note that, you know, there's a mouse study where Dr. Pearson has eliminated it because he didn't think the dose was relevant.

And the highest dose in mice was 302 milligrams per kilogram. And I'm looking at some

of the others.

Some of these don't necessarily -- oh, here we go.

Rats. He eliminated Saad, et al. 2017, for the same reason and they gave 250 to 500 milligrams per kilogram. I believe that's to rats.

And then he eliminated another study. Let's see if it's rats or mice.

BY MS. HUNT:

Q Okay. Dr. Powell, I've been really patient with your answers, but I just have to instruct you, if you can please focus on the question that I'm asking, that would be really helpful in getting us out of here at a reasonable time.

So you -- are you saying you don't have a problem with allometric scaling, but you do have a problem with the 10X safety factor?

A Well --

MR. PADGETT: Object to form.

THE WITNESS: It's not a matter of having a problem. I mean, I told you I picked a conservative cutoff that's relevant to human dosing in rodents and with a safety factor.

So I was conservative in my estimation, and I find it striking, again, that, you know, there's -- I

don't even -- I can't even ascertain what the cutoff was for Dr. Pearson in this study, so insofar as he's eliminated high dose mouse studies, then it's hard to answer your question about whether the studies altogether gave higher doses to rats than to mice when you've eliminated the high-dose mouse studies.

BY MS. HUNT:

Q Do you understand that I'm not asking you about Dr. Pearson's opinion right now, I'm asking you about your opinion?

A Well, you're asking me my opinion about his -- about rats and mice and the studies, and you're excluding multiple studies in mice that use higher doses, so it's hard for me to answer your question when I'm looking at a document that doesn't include all the studies.

Q Okay. So we're going to look at the transcript together.

The question that I asked you is: Are you saying you don't have a problem with allometric scaling but you do have a problem with the 10X safety factor.

That's the question we're currently on, Dr. Powell.

MR. PADGETT: Same objection.

BY MS. HUNT:

Q So if could you -- if you could answer that

question.

A I thought I did.

Q Well, you started talking about Dr. Pearson. I'm not asking about Dr. Pearson. I'm asking you, Dr. Powell. And you know what, I think I can make this easier by going back to the text of your expert report.

Why don't we look at what's been marked Exhibit as 201, page 24, top of the page, paragraph 54.

Okay. For purposes -- and this is the very top of the page, beginning at that paragraph.

"For purposes of nonclinical rodent study dosing, the 2005 FDA allometric scaling guidance document used by plaintiffs' experts to calculate a general human equivalency dose of 6.2X for rats and 12.3X for mice is not appropriate or accurate for acetaminophen."

Did I read that correctly?

A You did. And the reason that's written there is because that particular document wasn't designed for that. It had nonbinding recommendations for translation from rodents to first-in-human studies.

Q Okay. But what I'm asking about is not the document itself, but the underlying principle of allometric scaling, and what I'm trying to figure out is, to the extent that researchers studying the developmental neurotoxicity of acetaminophen used allometric scaling to figure out a

translationally relevant dose.

Do you have a problem with that approach, or is it the use of this FDA document that you have a problem with?

MR. PADGETT: Object to form.

THE WITNESS: Good question.

This particular sentence refers to the 2005 FDA allometric scaling guidance document is not appropriate.

The truth is, you know, allometric scaling is a first pass for a drug when you don't know what's going on in humans. But in this drug, we know what the doses and what the levels are and what the areas under the curve were, so the most appropriate way to do it would be to look at the doses that, when given to mice or rats, reach a concentration in their bloodstream that is a peak of around a maximum of 132 micromolar, and a steady state of around 50 to 60 micromolar, if my memory serves.

So it's not that I have a particular problem with allometric scaling. In fact, if you're using a single dose, I think it, you know, it's a reasonable approximation, and I've used the higher cutoff in my report.

BY MS. HUNT:

Q Okay. I'd like to show you what I've marked as

Exhibit 217.

(Powell Deposition Exhibit 217 marked for identification.)

BY MS. HUNT:

Q Dr. Powell, do you know what Ofirmev is?

A Ofirmev?

Q Mm-hmm.

A It sounds like an abbreviation they're using. Can you spell it out?

Q So if we want to go to what's been marked as 217.3. First paragraph. I'll just read it to you.

"This review provides comments from the Division of Medication Error Prevention and analysis regarding potential medication error issues identified with the proposed container label, carton and insert labeling for Ofirmev, acetaminophen, injection."

Does that refresh your recollection as to what Ofirmev is?

A It's a brand name --

Q Yes.

A -- for an injectable form of acetaminophen.

Q Okay. And --

A Can I clarify one point?

Q I'm sorry, but no. You can if it's responsive to a question.

A It is. I just want to make it clear that there's more than acetaminophen in Ofirmev. There are additional, I believe antioxidants, if I'm not mistaken, but I'm not 100 percent sure.

Q And why do you think that they believed antioxidants in the IV preparation of acetaminophen?

A Presumably to protect the liver from damage.

Q And is that, in part, because acetaminophen causes oxidative stress?

A I would say that it's -- well, first of all, I don't like the term "oxidative stress."

Second of all, in normal dosing, I'm not aware that there's depletion of glutathione in the liver, and complete depletion of glutathione in the liver, and it would be because one of the mechanisms that is thought to underlie hepatic insults is due to oxidative stress, especially given that the liver makes a lot of the enzyme CYP21E compared to the brain.

Q But the liver can regenerate, right, and the brain can't?

A We've already discussed that, yes.

Q Okay.

A To some degree, that's true.

Q And certainly they're not including an antioxidant preparation in this IV formulation of acetaminophen for

recreational purposes, right, there's a reason for it?

MR. PADGETT: Object to form.

THE WITNESS: I have no idea what they're thinking was behind that.

BY MS. HUNT:

Q Okay. So you think they may have just randomly included an antioxidant in this preparation of acetaminophen?

A No. I don't why you're asking me that because I didn't say that, but no.

Q Okay. But you don't know why?

A Well, I think it's to protect the liver.

Q Okay. From -- and I know it's a term you don't like, to protect it from oxidative stress?

A To protect it from the possibility that it could, in theory, decrease the level glutathione, and so out of an abundance of caution they added it, would be my presumption, but it's just that presumption.

Q Okay. And does this appear to you to be part of the FDA's review process for approval of the Ofirmev label?

A Honestly, I don't know. I've never seen any of those documents until today. As far as I remember, but I don't dispute that if that's the case.

If you're representing it accurately, I don't dispute it. I just don't know.

Q Okay. Let's go to -- just a second.

Let's go to what's been marked as 217.35.

And do you see the highlighted language on this page, Dr. Powell?

A I do.

Q Does this appear to be describing a reproductive toxicity study of acetaminophen?

A I'm just going to read it for a second.

Q Take your time.

A In part, yes.

Q Okay. And do you see here where it discusses -- it's the second sentence.

"These doses are approximately .42, .85 and 1.7 times the MHDD respectively based on body surface area."

Did I read that reasonably correctly?

A You read it correctly. And I don't know what MHDD stands for in this context.

Q Okay.

A It may say -- maximum daily human dose.

Q Correct.

A So, yes, they are giving all of -- giving a maximum dose in the food to these animals.

Q And when you calculate a dose based on an animal's body surface area, would you agree with me that that's a form of velometry?

A I think so. But I'm not an expert in velometry, but that sounds like one of the criteria they use in velometry, yes.

Q Okay. I'd like to go back to page -- what's marked as page 217.2, and that's just the cover page, I think, for this document.

Do you see the date, it looks to be September 13th of 2010?

A Yes.

Q Okay. And so does -- does it appear to you, based on this document, that the FDA was using allometric scaling to determine the human safety of acetaminophen as of 2010?

A Well, first of all, I can't speak to that because it doesn't say anything about who did this study in the paragraph that you highlighted that I read on page 217.35.

Second of all, I mean, yeah. I don't even know if they -- I mean, they don't have a reference either to that, so I don't know where it comes from.

Q Okay. Do you agree with me that mice and rats have different body surface areas?

A I do.

Q And did you take that into account anywhere in your expert report when you were determining the 200 mgs per kg dose, which you applied to both rat and mouse studies?

A I would say, yes. Because the first thing I did

was use the allometric scaling without the correction factor to figure out what the dosing should be.

And again, in rats, it was around, for a human dose, the maximum would be around 90 milligrams per kilogram to a rat.

And it would be around 100, I think around -- close to 150 milligrams per kilogram, maybe a little more or less, but that's roughly what I determined for a mouse.

And again, I increased my cutoff above both of those maximum single doses on allometric. And for mice it's above the liver toxicity dose and, of course, as we mentioned, for rats, I didn't think the toxicity dose was relevant because they're particularly resistant, as far as I read in the literature.

Q And so -- I'm sorry. You're saying you did the math and the allometric scaling for a rat dictated 90 mgs per kg, but for a mouse it dictated 150 mgs per kg?

A That's what I said.

Q Okay.

A But I'm happy to calculate it out. So if the maximum dose for a normal human is a thousand milligrams and you divide that by a standard human being of 70 milligram -- 70 kilograms, not pregnant human beings, but average human being, you get a single dose of 14.3 milligrams per kilogram and at two Extra Strength Tylenol dose in a human.

If you multiply that by 6.2 or 3, let's do 3 just to be conservative, because I never can remember which is which, you get 90 milligrams per kilogram for a rat.

And if you do the same thing, let's just say 14 milligrams per kilogram times 12. -- I'll do 3, it gives you 172.2. And my cutoff is 200 for both. So I think that's a very conservative, lenient interpretation, based on allometric scaling and my understanding of the dose that causes -- that can begin to cause liver toxicity in mice, is 150, so I think I was quite conservative.

Q So you did use allometric scaling in coming to your ultimate dose opinion?

A I used allometric scaling at first, and I used liver toxicity in mice, and I came up with a number that I thought was particularly conservative.

I mean, I'll point out that when I started this process, I included 99-plus studies, some of which used, you know, way, way, way, really high doses, and I had no a priori knowledge of what the consensus or what the Court would rule is the cutoff or whatever it is.

So I was as conservative as I thought was reasonable, and I think the idea that, you know, the four or five studies that both Cabrera and Pearson included where the rats gets 350 milligrams per kilogram per day is high --

Q Do you --
A -- for a human dose.
Q Do you explain anywhere in your report where you made those calculations?
A Let's see. I explained something about allometric.
I see my -- where I note that other people failed to provide any details quantifying their dose levels.
I'm too far down in my report to do this. I should go backwards. There it is. There's part of it. Let me see if I do --
Q I guess I'm just confused because you said that those conversion factors were inappropriate and inaccurate for acetaminophen, but now it sounds like you used them, in part, to come up with your opinion, which, of course, is fine with me because that's what our experts used, in part, but I just want to see where that is in your report, I guess.
A Yeah. So I think I -- I mean, as we already talked about, that FDA document I think is inappropriately used because of what it says at its face.
And remember, it was cited by plaintiffs' experts, and so I looked at it and read what it was for, I read the whole thing, but I read what it was for, and it clearly says what it's for.

Q So --
A And what it -- and then I noticed that, in the end, there was a lot of talk about that this is done all the time and everything, but I didn't find a reference to that in plaintiff's experts' reports.
But again, what I did was -- and I don't explain exactly how I came up with that number, but I think I do explain that it is a conservative estimate.
Q Okay. But the math --
A And I state -- I'm sorry.
Q No, no. Go ahead.
A And I said what the value is.
Q And -- but the math that you did here today, that's how you came up with those numbers.
In other words, we should go off what you're telling us now rather than -- because I don't see it in the report, so I'm just trying to understand.
A Well, you've seen my --
MR. PADGETT: Object to form.
THE WITNESS: -- cutoff, so I think it's reasonable to include less than 200 milligrams per kilogram. I think it's conservative to do so in both rats and mice.
I'm not sure how else to say it than that.
BY MS. HUNT:

Q Okay. And you -- you said that you felt it was inappropriate for them to cite to that FDA document because it's for first-in-human trials.

But you don't have a problem citing to Gurusamy, which is also for first-in-human trials?

MR. PADGETT: Object to form.

THE WITNESS: What I would say is that was one of multiple resources that I used, and so I have no problem citing it because it's for translating from mice data into humans.

And in this case, this is a dose translating from mice into humans with a tenfold corrective factor. So I think we're comparing apples to oranges.

But in any case, I used a conservative number, and I say exactly what that number is.

BY MS. HUNT:

Q Okay. And where do you take into account in your report the differences in APAP metabolism across species?

A In my determination of a conservative threshold of 200 milligrams per kilogram, which is higher than the liver toxic dose in mice and higher than the allometric scaling dose in mice for a maximum human dose and higher than an allometric rat dose.

Q Okay. So your testimony is that using the same dose for rats and mice is how you took the species'

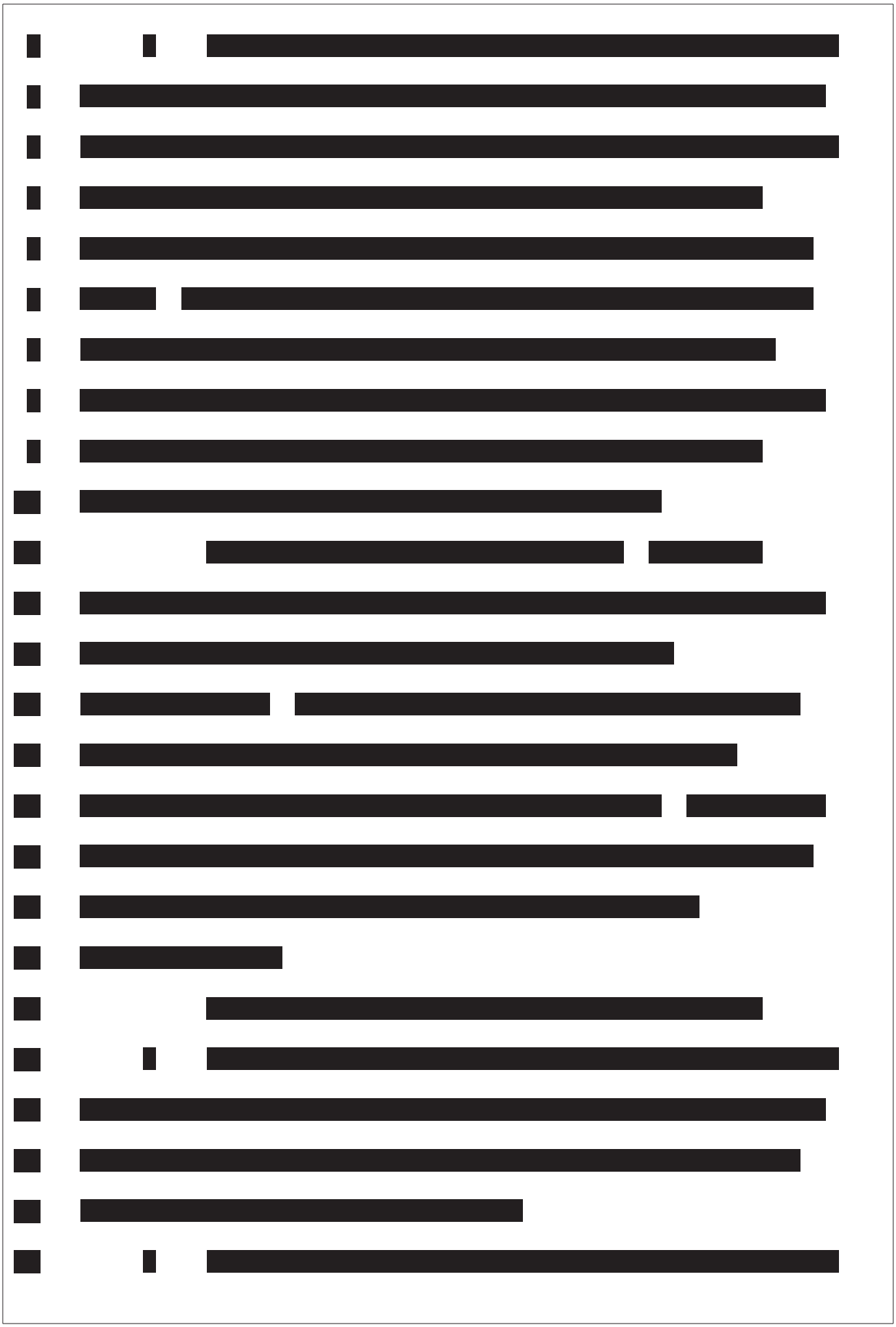
differences into account?

A No.

MR. PADGETT: Object to form.

THE WITNESS: That wasn't my answer.

BY MS. HUNT:



BY MS. HUNT:

Q Okay. Yeah, I'm just doing my best here, Doctor.

A I'm not complaining.

Q And is it -- is it -- is it a fair summary to say that it's not just that species are different sizes, but they actually metabolize the chemicals differently?

MR. PADGETT: Object to form.

THE WITNESS: Well --

BY MS. HUNT:

Q They metabolize acetaminophen differently?

A With respect to the liver, I would say that they

probably do metabolize these differently and -- yeah, sure.

Q So is it your belief that although the liver metabolizes acetaminophen differently across these different species, other tissues and organ systems metabolize it the same?

A I'm sorry --

MR. PADGETT: Object to form.

THE WITNESS: I didn't catch the whole thing.

MS. HUNT: Oh, no, it's okay.

THE WITNESS: I think because of the AC.

BY MS. HUNT:

Q So is it your belief that although the liver in these two different species metabolizes acetaminophen differently, other tissues or organ systems in rats and mice would metabolize acetaminophen the same way?

A Well, I --

MR. PADGETT: Object to form.

THE WITNESS: It was a little ambiguous, but I would say this.

I don't really have any a priori knowledge of how the rodents are metabolizing acetaminophen in other organs, other than the liver.

And I have some understanding of what I think might be going on in the brains, but there's much less data about that in the rodents and in the humans.

BY MS. HUNT:

Q Are rat brains and mouse brains different sizes?

A They are.

Q Okay. And are they otherwise anatomically different at all?

A In some --

MR. PADGETT: Object to form.

THE WITNESS: In some ways, yes. In many ways, no, but they're different.

MS. HUNT: All right. I'm happy to take a break now.

THE WITNESS: Thanks.

THE VIDEOGRAPHER: Off record. 3:12 p.m.

(Off the record at 3:12 p.m.)

THE VIDEOGRAPHER: On record. 3:35 p.m.

BY MS. HUNT:

Q All right. Dr. Powell, I want to go back to your expert report again.

And I'd like to turn to page 27, and at the bottom of page 27, under "Methodology," you describe your search terms, and I think it continues onto the top of page 28; is that fair?

A Yes.

Q Okay. And is there a reason that your search terms didn't include anything about gestation or pregnancy?

A Yes.
Q Okay. Tell me about that.
A Well, my first literature search I wanted to be as inclusive as I possibly could be and then exclude papers on my own manually.
Q Okay.
A So that I didn't end up with too few or too many articles.
Q Okay. And do you have a complete list somewhere of what articles came back as a result of your literature search?
A I do not.
Q Did you, at some point, have a complete list of articles that came back as a result of your literature search?
A Well, I had the result of my search on the computer, and then I went through all the papers.
Q Okay. And so you deleted the list, or it got merged into a draft or what?
A I didn't delete the list. I didn't print out the list. I went through the list and looked at the papers.
Q Okay.
A And then I closed my window and I kept the papers that I thought were relevant and melded them with some papers that I was provided in -- at the outset of this case

by defense attorneys, as I say, at the last sentence of the paragraph 28. And then I began reading them.

Q Okay. So as usual, Dr. Powell, you're 10 steps ahead of me.

In that next paragraph, paragraph 61, which is on page 28 of your report, you say at the end of that paragraph that some articles were also separately provided to you by the defense attorneys in this case; is that accurate?

A Yes.

Q And do you know sitting here today which studies came from your search and which studies were provided by lawyers?

A No, I think there's a lot of overlap, let's just say, between what I did and what I got from --

Q Okay.

A But not 100 percent, I don't think.

And then, of course -- well, I found other articles as I read the literature -- citations in some of the articles led me to additional articles.

Q Okay. And you say in paragraph 63 that you reviewed each study and you noted several categories of data, which I think continues onto page 29; is that right?

A Yeah.

Q So did you have a chart or something similar that had these annotations about each study?

A A chart or something that did annotation of these studies.

Oh, so I noted all these things in draft versions of my report and then turned them into paragraphs.

Q Got it. Okay.

I think we can turn away from the report for a second.

When were you first contacted about being an expert in this case?

A I believe it was on or about February the 22nd, 2023.

Q Okay. So all of your opinions in this case you came to in the last six months; is that fair?

A Six months and roughly a week, yeah.

Q Okay. And who initially contacted you?

A I think it was David Cohen at Butler Snow.

Q Okay. And how did you decide on an hourly rate?

A I have a -- well, I have a colleague that does this quite a bit, and I used his hourly rate.

Q Who's that colleague?

A I'd rather not say if I can avoid it, but I don't know if I can or not, to be truthful.

Q Is it someone involved in this case?

A Oh, no. Not at all.

Q And I think as of June, you had billed about 123

hours. Does that sound approximately correct to you?

A I don't know. It was about $98,400 worth of hours at $800 an hour.

Q Okay. And of those hours, how many would you estimate you've spent reviewing the studies?

A Countless. I mean, I really have no earthly idea.

It takes a long time to read -- the amount -- the number of articles that are in these two binders carefully. And I want to point out I read them once and that gave me a good feel, and then I read them for, you know, several -- I went through them several times for various reasons while preparing my report.

Q You're preaching to the choir, Dr. Powell.

A I'm certain of it.

Q And how many hours did you spend reading about acetaminophen and its effect on neurodevelopment before you decided to be an expert for the defendants in this case?

A Ooh, interesting question. About, I mean, I think what -- if memory serves, I looked at it -- an e-mail, and then I may -- I can't remember.

I think I responded to that e-mail, and then I think I agreed, you know, said, you know, agreed to a call. And then while I was talking on the phone and learned more about what the case was about, I did a quick Google search to see, you know, so maybe 5 minutes, 10 minutes.

Q Okay.

A But I don't know. I don't recall the exact date when I -- well, I agreed on the date of the call, and then I don't know what you consider the formal agreement agreement, but that's -- I just don't recall when that formal formal, I don't know when it becomes formal, to be honest with you.

Q And did you have to submit an external activity form to UAB in connection with your work on this case?

A Yes.

Q And did you get formal approval from UAB to work on this case?

A I did.

Q And I know in the past when you've testified as an expert witness, a portion of your income from that work has gone back to your lab.

Is that the case here?

A So, first of all, none of that money went to my lab, I wish it would have.

25 percent of those monies at University of Texas Southwestern Medical Center in Dallas -- actually all of the money that I received went to UT Southwestern Medical Center in Dallas, every penny of it. I signed the check over. They took it.

And then I got 75 percent back in paychecks, I think, twice a year, or once or twice a year.

Q Okay. And are you in a similar arrangement now at UAB or no?

A No.

MR. PADGETT: Can I just object that this relates to an agreement, and I've got the e-mails, back and forth between Jim Murdica and Mikal Watts that as far as compensation, there's an agreement that the only two questions to be asked about expert compensation were hourly rate and total -- total amount.

MS. HUNT: Uh-huh.

MR. PADGETT: And so that --

MS. HUNT: Okay. I'm happy to move on.

BY MS. HUNT:

Q Okay. Dr. Powell, going back to your report.

Is it fair to say that one of the -- one of the issues that you critiqued with the studies you analyze is failure to perform an a priori power analysis?

A Yes.

Q Okay.

A No. I change my answer.

One of them was failure to include in the paper a report of a power analysis which, in my view, is interpreted as it either wasn't done or it was done and not followed or it wasn't done.

And again, I eliminated no papers on that basis of

my analysis and is the basis of my opinions.

Q Did you review any publicly available grant or funding information about those studies that might have included a power calculation?

A I'm not aware that any public database would include those sections of any grant. So -- but I did not do that.

Q Okay.

A Because I wouldn't have come up with the answer.

Q Is it fair to say that every time you didn't see an a priori power analysis included in the paper's methods, that was part of your critique?

In other words, even if you suspected they may have done one, you critiqued the study if they didn't explicitly describe it?

MR. PADGETT: Object to form.

THE WITNESS: I don't remember. I don't remember where I put my report.

I don't know that I even have a list of papers that don't do a power analysis, who don't report a power analysis. I can't recall.

But what I do remember is that I don't recall any of the studies mentioning a power analysis of the ones that I reviewed, the 99 papers of in vivo rodent studies, I may be wrong about that, but I can't recall

that any of them contained that and, you know, I think that's totally fine for an exploratory study.

I think the reason I criticize it is because I was concerned that we're not using these to -- you know, in that -- in this arena, you know, those types of exploratory studies can generate hypotheses that require them to be tested and proven in a way that's rigorous.

So I don't -- I didn't eliminate any papers on that basis.

BY MS. HUNT:

Q Okay. And you don't always include an a priori power analysis in your own work, right?

A I don't. I typically do that for the exploratory studies where we're characterizing mouse models.

I would say that -- for when we do things like proteomics or genomix, where there's like thousands of things to test, we typically do correct for multiple comparisons, and we -- oh, you asked power analysis. I'm sorry. I'm answering the wrong question. You're right.

So power analysis. I often don't in our exploratory research.

Q Okay. And then I want to turn to page 47 of your report which, again, is marked as 201.

You have a section starting at the top of page 47,

and it continues through the middle of page 49, where you talk about proposed mechanisms in the Bauer, et al., reviews; is that right?

A That is correct.

Q Sorry, give me one second.

And when you say the "Bauer, et al. reviews," are you talking primarily about the consensus statement?

A In air quotes, that's what I put in the first sentence of that section, yes.

Q Okay. And your opinions in this section of the report, are they part of your systematic review that you described earlier with the search terms and the criteria, or is this a supplementary part of your expert report?

MR. PADGETT: Object to form.

THE WITNESS: Yeah, I wouldn't call it supplementary.

So I guess I would say that I read a lot of, you know, it's difficult to go through all the literature about all the ever-proposed mechanisms that might possibly be related to a drug.

So when I saw the Bauer, et al. reviews, I thought that was a reasonable place to start and say, okay, these are obviously things that are hypothesized to be potential mechanisms, and so I looked into them at the references in the Bauer, et al., and other

references, I think, and just wanted to go through them systematically, if you will, but it's not a weight of evidence or systematic review, per se, and review the literature and learn -- try to understand if there was valid, consistent, literature that supported these potential hypothetical mechanisms.

BY MS. HUNT:

Q Okay. Because you talk quite a bit in this section about, for example, anogenital distance, and that was not part of the list of search terms that we discussed earlier, right?

A That is correct. And this is in direct response to the question of plausible biological mechanisms, and I wanted to look at what they potentially were. And this was one that was highlighted by Bauer, et al., and has since been highlighted by some of the experts on the plaintiffs -- some of the plaintiffs' experts.

Q Could you have conducted a full literature search about the endocrine effects of acetaminophen, including issues like, for example, anogenital distance?

MR. PADGETT: Object to form.

THE WITNESS: I'm sure I could have.

However, it wasn't necessary because there have been tests of anogenital distance in autism, and they're not associated.

And I cite to it, or to review, I'm not sure which -- what articles they are, as I look at the numbers.

Go ahead.

BY MS. HUNT:

Q But in this section of your expert report, you didn't undertake a full review of all of the literature that might be out there.

You just read the consensus statement and then wrote your response to it; is that fair?

A To some of those mechanisms, yes. And then later, of course, I responded to some of those mechanisms that were raised by plaintiff experts.

Q Okay.

A I wouldn't call it supplemental, though, because I think it was not part of my amended report with rebuttal. Or it wasn't -- how do I put this?

Oh, I think you got a copy of my initial report, and then you got a copy of my initial report with the rebuttal. And I think the section was in the initial report, but I'm not -- I can't --

Q Okay.

A -- know 100 percent for sure, but I'm pretty sure it was.

Q Okay. But you didn't do, you know, for example, a

Bradford Hill analysis on acetaminophen and endocrine disruption as part of this analysis?

A In humans, no.

Q Okay. How about a full weight of evidence analysis on acetaminophen and endocrine disruption in in vivo animals?

MR. PADGETT: Object to form.

THE WITNESS: I know I did literature searches on that to find all the articles that I cite, which are multiple.

So I definitely read many articles on the subject and evaluated them.

BY MS. HUNT:

Q On endocrine disruption?

A Well, I cited 147, 151, 148 through 150, 153, 168 through 74.

So I read a lot of papers to ascertain the plausibility of this mechanism for causing autism spectrum disorder or -- and/or ADHD in humans.

Q Do you have those search terms?

A I do not.

Q Okay. So there's no way for me to go back and reproduce the search again if I wanted to?

A No. But you could look at the references I cite.

Q Okay. I want to talk a little bit about Baker

2023. I've marked that as Exhibit 244.

(Powell Deposition Exhibit 244 marked for identification.)

BY MS. HUNT:

Q Dr. Powell, I'm sure you've seen it a time or two. So, I believe you say in your expert report that they saw a decrease in locomotor activity and that that's an unexpected result for a rodent model of ADHD; is that fair?

A That wouldn't be the hypothesis and nor is it the hypothesis that Dr. Pearson outlaid when he discussed those types of tests in relation to ASD and ADHD.

MR. PADGETT: For the record, I'll object to Exhibit 244 because of the last paragraph appears to have been probably inadvertently completely covered up by highlighting, at least on my version.

MS. HUNT: Oh, did I get too excited highlighting? Sorry, Bill.

THE WITNESS: Let me get a clean copy.

MS. HUNT: Your objection is noted.

MR. PADGETT: I'm sure I have a clean copy.

BY MS. HUNT:

Q All right. And actually, we can turn back to your expert report for a moment. That's probably easier. If we go to page 30 of Exhibit 201. I want to talk a little bit about what's at the very end of that page.

You say: "Of note, the lack of changes in pup ultrasonic vocalization is not consistent with expectations of a proposed ASD model. Decreased social communication is a core feature of ASD and a decrease in social communication in mice is hypothesized to be manifest as decreased USVs."

Did I read that correctly?

A Yes. And I -- you pointed out, without pointing it out, that when I said the lack of changes, I must have meant lack of decreases. But go ahead.

Q Okay.

A It's an error.

Q And have you ever published on USVs?

A Maybe once or twice, yes. We haven't done any recently for various reasons.

Q I'd like to look at what's been marked as Exhibit 251.

(Powell Deposition Exhibit 251 marked for identification.)

BY MS. HUNT:

Q And before we fully dive in here. Is it your opinion that pup ultrasonic vocalizations in mice are analogous to social communication in humans?

A I would say that --

MR. PADGETT: Object to form.

THE WITNESS: -- my opinion has evolved on

this.

Many people -- some people, excuse me, not many. Some people have argued that ultrasonic vocalizations in rodent pups or rodent adults during mating have some relevance for autism spectrum disorders in that they may be, in some way, have some tiny bit of face validity with human language communication.

And what I would say is, I sort of believe that that might be reasonable as an argument in the past, and my thinking has evolved over time on that.

MS. HUNT: Okay.

THE WITNESS: I think it's controversial, whether it has any relevance whatsoever, but insofar as it does have any inkling of face validity, it is hypothesized would be -- hypothesis would be decreased or altered in the character.

BY MS. HUNT:

Q Okay. And I want to also pause for a second on -- you say here "decreased social communication is a core feature of ASD."

Does the DSM require somebody with ASD to have decreased social interaction?

A The DSM-IV main criteria are, number one, deficits in social communication and related social parameters and

deficits or -- I don't remember what it says about that actually.

But in terms of communication, I believe the word is "deficits," and then -- yeah.

Q And --

A That would imply a decrease.

Q And clinically -- okay.

So your position is that deficits implies a decrease and not just abnormal social communication?

A Well, deficits would be abnormal.

Q Okay. So --

A But that's -- I'm just telling you the word in the DSM-V -- excuse me. I keep saying -- to the extent that I say "DSM-IV," let me just tell you that I grew up on DSM-IV when I was in training, at certain times in my life, I think we were DSM-III for a while, then DSM-IV, now we're in DSM-V.

If I ever have said DSM-IV instead of DSM-V, I mean DSM-V. I apologize.

Q I totally understand.

But -- so is it your position that the DSM requires decreased social behavior or just abnormal social behavior?

MR. PADGETT: Object to form.

THE WITNESS: It's my testimony that the

first word for that criteria and others in ASD is deficits.

BY MS. HUNT:

Q And aren't there clinical presentations of ASD where a patient might actually be very social but just in an inappropriate way?

A In autism spectrum disorders. I don't know how to describe it in a way that makes it easily understood, but I would say that there are patients who have deficits in social communication who may talk about subjects that are tangential to the topic and that's a manifestation of their restricted interests.

Q And they might not pick up on social cues, for example, that the other person --

A They have deficits in understanding social cues, yes.

Q Right. So they might not pick up that the other person in the conversation would like to move on and they're still talking about mice, for example?

A What's the question? Sorry.

Q Just -- that's okay. We can keep -- we can keep it moving.

Okay. So I'd like to talk to you a little bit about this paper that I marked as Exhibit 251.

(Powell Deposition Exhibit 251 marked for

identification.)

BY MS. HUNT:

Q Do you recognize this as a paper that you're the last author on?

A Yes.

Q Okay. And is this paper about a Shank3 mouse model of autism?

A It is.

Q Okay.

A Oh, no, it's not. It's a model -- it's a mouse model for autism caused by a Shank3 loss of function mutation.

To the extent that I ever have said model of autism or agreed that you -- to you calling it a model of autism, I have to correct the record and say that we now no longer talk about models of autism, although that's the title of this paper.

We talk about animal models for studying aspects of autism. And that's sort of an edict from the National Institutes of Mental Health Director, Josh Gordon.

So when I first started this, I said mouse model of autism because it's a short term for mouse model of a genetic cause of autism, where we can learn something about potential negatives.

But go ahead.

Q Okay. So I'd like to move to what is marked as 251.24.

And do you see the chart, I think it's labeled as D in the top right corner of that page.

A 24, the chart? 251.24 is where you're on?

Q Yep.

A And you're asking me if I see a chart? I see -- the graph. Yes, sorry.

Q Yes.

A I'm not trying to be --

Q No, it's okay.

A -- picky.

Q That' okay. Okay.

And is the chart labeled as D, a chart that describes pup ultrasonic vocalizations?

A I believe it is.

Q Okay. And what does WT stand for?

A Wild type. Typical.

Q Yeah. Right.

So a wild type mouse is a typical mouse that hasn't been genetically --

A Altered.

Q -- modified, right?

A Correct.

Q What does HET stand for?

A It means heterozygous, which means that one copy is, in this case, mutated.

Q Okay. And how about KO?

A KO means two copies are mutated.

Q Okay. And if we look at that chart, the y-axis is the number of calls every five minutes?

A It is.

Q Is that fair?

A Yes.

Q And the x-axis is the postnatal day?

A It is.

Q Okay. And so it looks like the mice that were genetically modeled to have some features of autism, I'm sure I'm disappointing Dr. Gordon, whoever he is.

Those mice, it looks like, had increases in the number of calls on postnatal day 4, 6, and 8, as compared to the wild type mice; is that right?

A That's correct.

Q Okay. And then you say -- below Figure 6, in the highlighted text, both heterozygous -- and KO stands for knockout?

A Yeah.

Q "Both heterozygous and knockout mice display abnormalities in the number of ultrasonic calls following separation from their mother early in life. At age

postnatal day 4 and postnatal day 6, knockout mice display an increase in number of calls compared to wild type mice, while heterozygous mice display increased calls at postnatal day 4 and postnatal day 12."

Did I read that correctly?

A That's correct. They would have had increased ultrasonic vocalizations in this case and we reported it.

Q And this study is from 2016; is that fair?

A It is.

Q And this study was performed outside the context of litigation, right?

A I hope so.

Q And so is there a reason why in that study you don't say what you said about Dr. Pearson's paper that the decreased social communication is a core feature of ASD and a decrease in communication in mice is hypothesized to be manifested as a decrease in ultrasonic vocalizations?

A Well, I'm not sure I didn't say that.

MR. PADGETT: Object to form.

THE WITNESS: I'd have to re-read the papers. Is there a place that you can point to where I said otherwise?

BY MS. HUNT:

Q Well, Dr. Powell, it's your paper. I'm not sure I can help you with that.

A I'm not asking for help. I'm happy to read the whole paper and see if I said anything to that effect. If you think it's not in there or is in there in a different form, I'm happy to look at it and tell you the answer.

Q Let's go back to your expert report for just a second.

On page 31 of your expert report, which again, is 201, you continue talking about the Pearson study.

You say: "Male pups actually demonstrated increased USVs at one point compared to controls. Another finding that is opposite of what would be hypothesized in an animal model for ASD."

Did I read that correctly?

A Yes. And that's exactly right.

I'm happy to explain. What we did in this study was take a known cause or try to replicate, reproduce, a known cause, a genetic cause of autism spectrum disorder, and when we do that and we learn that there's any behavioral abnormality of any face validity or change that's related to autism, we've learned absolutely nothing.

And I say this in every talk that I give. That we didn't already know. Because we already know in this case that mutations in the Shank3 gene cause autism spectrum disorder in humans.

And so in our studies, we look at behaviors, and

the general naive people expect them to look exactly like an autism person, and you cannot diagnose autism spectrum disorder in a mouse model.

So the purposes of our studies are to use the known cause and try and understand what's wrong with the brain and then if that might have some relevance and we can reverse it, then we'll look at that reversing that dysfunction in the brain and then see if that affects any of the behaviors.

And so in terms of behavior and what we're studying for mechanisms, I am -- and our lab remains agnostic as to what the expectations are, and let me tell you why.

It's because we already know what the cause is and that it is a cause in humans.

When you don't know a cause and you're talking about causality using rodents. Well, first of all, let me just say, if I tried to take a gene and pull it out of the genome and it had no relevance to humans and no causal relevance to ASD, and I put it in a mouse model and it looked exactly like that mouse study, it had all the face valid features of ASD, I would never be able to publish a conclusion that says this supports the concept that a mutation or loss of this gene in humans is a cause of autism spectrum disorder, period.

Q Right. So now we're back to it's important to know what the causes are of autism in humans, right, as you interpret the data in animals?

A In my work, we know it's a cause most of the time, and we don't necessarily look for face validity to support a cause. We don't look for face validity or any behavioral abnormality to support a cause, if it's a known cause.

We try to ask the question, if you model that cause, what happens to brain function and how might we fix it.

Q But you believe that neurotoxicologists like Dr. Pearson have to achieve face validity even though you don't?

A Well, you can --

MR. PADGETT: Object to form.

THE WITNESS: Well, no, that's incorrect. That's an incorrect characterization of my belief.

Insofar as the mouse studies, where acetaminophen is given to pregnant dams, and outcomes are tested in terms of behavior, if one wanted to even attempt to demonstrate that that supports causality in any way, shape, or form, which I don't believe it ever would, then the only thing that some people might actually believe indicated that it has any relevance at all to causality of autism spectrum disorders in a

human, would be face validity.

And I don't think that would -- and basically, I don't think that supports causality because mice can't have -- they don't have human behaviors, they don't have human interactions, they don't have almost -- they can't lose their cell phone or their keys. They don't have deadlines to miss. They don't have homework.

So you can't have a mouse that has autism, and that's the director of the National Institutes of Mental Health's position, Dr. Josh Gordon.

Q So it would be --

A We've agreed for a long time about that. And you'll never -- in any of the papers that come out of my lab, my laboratory, where I'm the last author, I'm not sure you'll find that we argue causality based on behavioral findings.

Q So you're saying it would be impossible?

A To do what?

Q To find causation in animal behavior studies related to acetaminophen as a developmental neurotoxicant?

A That's not what I said.

MR. PADGETT: Object to form.

THE WITNESS: I'll say it again.

What I mean -- what I said was very clear.

With respect to acetaminophen being -- being allegedly causal of autism spectrum disorder, or ADHD, as a diagnosis in humans, the mouse model behavioral does not help with supporting the causality in human because mice cannot exhibit those human behaviors and they cannot be diagnosed with autism.

I think every expert on this case has written words -- most experts in this case who think about animal studies have written that in some way, shape, or form, that mouse can't be diagnosed with autism spectrum disorder or ADHD.

BY MS. HUNT:

Q Is there a reason, in describing Baker 2023, that you didn't talk about the RNA sequencing data?

A Yes.

Q Can you explain why you didn't talk about it or evaluate it in your report?

A Well, I read about it, and I didn't find it particularly relevant in providing any evidence of causality or biological -- plausible biological mechanism in a human.

And so what we're talking about is a paper in which the word "neurotoxicant" and the conclusion that acetaminophen is a neurotoxicant, cannot be found in this paper, and yet Dr. Pearson's perfectly willing to testify that it's a neurointoxicant, but he won't put it in his

peer-reviewed paper.

Second of all, he states clearly in his paper, in his conclusion somewhere, that these are hypothesis-generating experiments and they do not -- and he never in this paper says that this concludes that this paper demonstrates that there's increased oxidative stress or DNA damage in a rodent model.

Q Did you say anything about RNA sequencing in that last answer?

A I did.

Q Okay. Can you explain to me why the RNA sequencing data, gathered in Baker 2023, is irrelevant to causality and biologic plausibility?

A I'd be happy to. None of the genes that change on the list of eight actual genes that increased in the brains of the fetuses, none of them are known to be causal of autism spectrum disorder, or ADHD.

And if -- if you'd like me to, I can explain the -- all the shortcomings of the subsequent analysis which generates multiple pathways based on some primary literature that's hard to find, but the bottom line is, when you have eight genes that change in a statistically significant manner, the next step conceptually is to -- in this type of a genome wide gene set enrichment analysis, you take all of the changes with a certain cutoff that none of which -- only

eight of which are statistically significant, and then you feed them into a program that has bio -- it spits out biological pathways, and -- that are overrepresented in those changes that aren't statistically significant to begin with.

And so all that does is generate a hypothesis that hasn't been tested, to my knowledge.

Q And do you explain any of that in your expert report?

A I do not.

Q Okay. Since we're talking about experts using different language in and outside of the context of litigation, I notice that you use the phrase "cherrypicked" a lot in your expert report.

If I told you that you used it five times in your expert report, would that sound about right to you?

A I don't know, but it wouldn't surprise me.

Q Okay. Is that a phrase you've ever used in your academic publications?

A No.

Q Have you ever used that phrase in any of your social media posts?

A I don't think so, but I'll point out that that's not a conclusion about this case. It's a characterization of ignoring one set of data and using only the data

selectively that supports your opinion, and that's something that I've used in conversations with other scientists, yes, but, no, I don't -- it's not reaching a conclusion that I'm stating. It's just characterizing that concept of picking data that supports but ignore data that doesn't support your conclusion.

Q As you sit here, can you point to a single written document where you've used that phrase outside the context of litigation?

A No. And again, it's not a scientific term or a scientific conclusion, which is in contradistinction to the answer you're referring to that I gave earlier.

Q You also -- if we can look at page 86 of your report. There's some other language I wanted to ask you about.

You were talking about -- this is at the top of page 86, you were talking about Beck 2001, and the controls, and you describe a process called gavage.

And your definition for gavage is grabbing the animal roughly by the nape of the neck and forcing a tube down the throat and into the esophagus, slash, stomach.

Did I read that reasonably correctly?

A You did. And if you've ever done it, that's exactly the only way you can do it without getting bitten by the mouse.

Go ahead.

Q Okay. Is grabbing the animal roughly a requirement of performing gavage?

MR. PADGETT: Object to form.

THE WITNESS: I would say that if you don't grab -- I've taught many people how to scruff a mouse, which is grabbing the animal roughly by the nape of the neck in a way so that it cannot turn its head and bite you and causing you to then fling the mouse across the room, curse loudly, and hurt the mouse worse than you otherwise would have.

So it's unethical not to grab the animal roughly the nape of the neck because it will bite you and you will respond reflexively.

BY MS. HUNT:

Q Okay. And another piece of language I want to ask you about, moving back earlier in your report to page 4, paragraph 7.

You say: "Overall, plaintiffs' experts' opinions are based upon flawed methodologies and unscientific speculation."

And I know you disagree with the ultimate conclusion of the experts who testify for plaintiffs, but are you opining that Bradford Hill, for example, is a flawed methodology?

A What I was referring to -- no.

What I was referring to here is that weight of the evidence scoring system of Dr. Pearson, which is in no way explained and which was, in my opinion, misapplied, and that's what I mean -- that's part of the things that I've outlined later in my report about flawed application of the methodologies.

Q Okay. So you don't -- you don't have an issue with Bradford Hill or weight of evidence.

You have an issue with how they were applied or interpreted by the experts on the other side of this litigation?

A How they were --

MR. PADGETT: Object to form.

THE WITNESS: How they were applied in practice.

For example, consistency, which was talked about in most of these experts' reports on the plaintiffs' side for sure, talked about consistency, which refers to reproducibility, replication, and no -- aside from speaking of it, they don't give a lot of weight or credence to the fact that many of these findings are either unreplicated or contradictory in nature.

BY MS. HUNT:

Q Okay. Does your expert report have a causation opinion in it?

MR. PADGETT: Object to form.

BY MS. HUNT:

Q In other words --

A It has a causation opinion with respect to the rodent literature, and -- well, that's -- it's in here. Let me see if I can search it real quick.

93. Paragraph 93. "In sum, after a thorough and systematic review of the existing literature on effects of acetaminophen on the rodent developing fetus, I can find no scientifically valid study that support a biological mechanism whereby acetaminophen might cause ADHD."

Q Okay.

A "Taken together, the behavioral and unbehavioral outcomes assessed in the systematic review of the acetaminophen animal scientific literature do not provide evidence of consistent, independently reproduced findings to suggest that the" -- "that maternal use of acetaminophen can cause ADHD or ASD in offspring."

And in this case, I'm referring to humans, which is the question of record.

Q And I think you actually say this again later in the report.

A It could be.
Q Let me make sure I find the page number.
Okay. So this is page 81, paragraph 177.
You say the -- at the end of that paragraph.
A Hang on. I can't listen to the question and find the place. Paragraph what?
Q Sorry.
A That's okay.
Q Page 81, paragraph 177.
A Page 81. 177. I'm at 81, almost. 177, got it.
Q At the end of that paragraph, you say: "The relevant question is whether appropriate doses of acetaminophen led to lasting changes in the developing brain that are consistent with the known causal pathologies of ASD or ADHD. Someone suggesting causation needs to demonstrate such a mechanism."
Did I read that correctly?
A You did. That's what it says.
Q So is your opinion that to determine general causation, when you see an association in human literature, human epidemiological literature, is it your opinion that you have to demonstrate biologic plausibility?
A No. What I meant was --
MR. PADGETT: Object to form. Go ahead.
THE WITNESS: What I meant in this particular

instance, and it's probably poorly worded, is that -- my understanding is that causation is a question by itself.

And I've stated, as you read, or I read, that earlier in their report, my conclusion from my analysis, which is that there's no evidence in the rodent literature that supports causality of ASD or ADHD in humans.

On the other hand, there's some sort of -- somewhere one has -- there's the idea that there must also be a plausible biological mechanism and there isn't, that I could find in the literature.

MS. HUNT: Okay.

THE WITNESS: That's what I meant to say.

MR. PADGETT: Can we take a short break soon?

MS. HUNT: Yep. Sure. In just a minute.

BY MS. HUNT:

Q Okay. And so I'm sorry if I'm being dense. I just want to understand.

Is your opinion that there should be biologic plausibility before someone can say this environmental cause -- this environmental --

A Exposure.

Q -- exposure, thank you. Leads to this outcome?

A That is not my opinion.

It's my opinion that -- I was given the task of reviewing whether the mouse models suggested causality or supported causality, and it's my opinion that they do not.

Separately, I was asked to comment on whether there's a biological plausible mechanism in this rodent literature whereby that might happen, and I did not find that.

Q Are you familiar with the Bradford Hill factors?

A After the last six months, I'm very familiar.

But no. I'm not 100 percent familiar with them, but I have a working passing knowledge of them, yes.

Q Did you ever have to learn them in school?

A I can't recall. I don't recall if I did.

I'm sure I might have, but I don't remember, to be honest.

Q Okay. As -- you know what, how about we take a break?

THE WITNESS: Okay.

MS. HUNT: I'm at a good stopping point.

THE VIDEOGRAPHER: Off record. 4:25.

(Off the record at 4:25 p.m.)

THE VIDEOGRAPHER: On record. 4:47 p.m.

BY MS. HUNT:

Q Okay. Dr. Powell, one of the things you point out in your expert report is that changes detected in

neurotransmitters might be transient and not permanent; is that fair?

A What I recall about my comments on neurotransmitter levels was that it doesn't -- it's not a marker of neurotransmission at all, or the function of synapses, or how neurons communicate with each other. It's the whole tissue level.

I don't remember saying that, but if you can point me, I'm happy to agree to it, if that's what I said.

Q Okay. And if a study like, for example, the Blecharz-Klin study measured neurotransmission, you don't have an opinion one way or another about whether those changes in neurotransmitters are transient or not?

MR. PADGETT: Object to form.

THE WITNESS: First of all, I would have to say that the -- but none of the Blecharz-Klin, in fact, none of the studies that I remember reviewing, as I sit like here today, measured neurotransmission, period.

And second of all, when you're talking about levels of whole tissue neurotransmitters, at one time point, I would say that would be an accurate statement if I said it.

BY MS. HUNT:

Q Okay. Did you use any methodology to determine that those changes were transient as opposed to permanent,

or is the assumption that because they were measured at one point in time they're transient?

MR. PADGETT: Object to form.

THE WITNESS: The way I came to that conclusion was I read the paper, and they were measured at one point in time. And so we don't know whether they are transient or not.

MS. HUNT: Okay.

THE WITNESS: That's what I can say.

BY MS. HUNT:

Q Switching gears a little bit, Dr. Powell.

Do you agree with me that, in general, the manufacturer of a drug should be concerned with determining any issues with its safety?

MR. PADGETT: Object to form.

THE WITNESS: Well, first of all, I think that all pharmaceutical companies should follow the appropriate laws and FDA guidelines, and I think that -- I think -- I don't know -- I mean, I know there's a lot of post-marketing surveillance that goes on in drug companies. In some cases it's mandated, they call it phase IV clinical trials.

BY MS. HUNT:

Q And is it particularly important if it's a drug that's being administered to pregnant women?

A Is what particularly important? Sorry.

Q The manufacturers acting responsibly over the drug safety.

MR. PADGETT: Object to form.

THE WITNESS: Yeah. I mean, acting responsibly is broad and vague, and so I'm not sure I can answer that question accurately.

What I think you're asking is: Should drug companies follow the laws and FDA regulations and processes, and I believe that they should, and I believe that that is our mechanism as a country for ensuring that drugs are as safe as they possibly can be and, of course, every drug has risks and benefits.

You can die tomorrow from an aspirin, from an anaphylactic reaction and, you know, when I read the list of possible side effects in patients, they often don't want to take a drug, and when I go back and I read them an aspirin side effects, or something like that, they -- they feel reassured because many of -- many of those issues can overlap with things that they feel very safe.

BY MS. HUNT:

Q Okay. And so that information that pharmaceutical companies provide to doctors and consumers, it's important that it be accurate?

MR. PADGETT: Object to form.
THE WITNESS: It's important that it be compliant with the FDA guidance and laws.
BY MS. HUNT:
Q Okay. But you don't care if it's accurate?
MR. PADGETT: Object to form.
THE WITNESS: I assume it's accurate.
BY MS. HUNT:
Q Okay. When you treat pregnant patients, do you ever have occasion to reference the FDA's pregnancy categories?
A Reference the FDA categories. I -- I have -- I look at them. I don't know what you mean by "reference," but I definitely look at them. So I'm familiar with it, at least the way they used to be.
I don't know if it's been changed from A, B, C, X, or whatever, but.
Q Would you agree with me that those categories have meaning in terms of what you might recommend to a pregnant patient or what a pregnant patient might ultimately choose to take?
MR. PADGETT: Object to form.
THE WITNESS: You know, I -- in my practice, I'm trying to remember if I've ever prescribed a drug to a pregnant woman without consulting an OB-GYN, and I

don't think that I have.

So I always make that decision, especially when I'm doing consults in the hospital. They're usually on the OB-GYN service, and I consult with them on the safety and pregnancy issue.

And, of course, I look it up myself and have some idea, so I don't, you know, so I can speak intelligently with the OB-GYN about the question and what I think should happen.

BY MS. HUNT:

Q Would it be okay with you if a pharmaceutical company misrepresented what pregnancy category a drug was in to a doctor?

MR. PADGETT: Object to form.

THE WITNESS: What was the word you used, would I be?

BY MS. HUNT:

Q Would it be okay with you if a company misrepresented the pregnancy category a drug was in to doctors?

MR. PADGETT: Object to form.

THE WITNESS: Well, I don't know the laws, but I don't think that's okay within the guidelines.

BY MS. HUNT:

Q Because you would want accurate information,

right, if you were going to recommend a drug to a pregnant woman?

A I would -- well, first of all, I would check with the OB-GYNs first, which is my routine practice, especially since I mostly work in the hospital setting.

But I would say that the pregnancy categories I hope would follow the laws and the regulations of the FDA and other authorities.

Q And it would behoove the manufacturer to know which category their drug fell into, right?

MR. PADGETT: Object to form.

THE WITNESS: I'm an academic neurologist, a neuroscientist. I've never worked in a pharmaceutical company in my life, so I don't have a lot of information on what they should or shouldn't do.

But insofar as would it behoove them, I think it would be in their interest to have accurate information, sure.

BY MS. HUNT:

Q Okay. Do you think that pharmaceutical companies can sometimes create bias around the safety of their products?

MR. PADGETT: Object to form.

THE WITNESS: I don't know.

BY MS. HUNT:

Q Are you aware that that phenomenon has been studied?

MR. PADGETT: Same objection.

THE WITNESS: I don't think I've read that literature.

BY MS. HUNT:

Q Are you aware of sponsorship bias?

A Sponsorship bias.

MR. PADGETT: Same objection.

THE WITNESS: I think if you're -- I'm not really aware of that term, but what I am aware of is, you know, we used to get a lot of pens and little books and they used to have stickers on them.

And I could never figure out the point of that, because I don't -- I never thought that it was affecting my prescribing practices. However, now we don't do that anymore, and so we don't have sponsorship bias these days.

If you mean by sponsorship bias, tchotchkes and swag and trips that, you know, to exotic places that I've never been on.

BY MS. HUNT:

Q Are you aware that there is a body of literature analyzing how replicated studies can be different depending

on who the financial sponsor is?

A I don't know that --

MR. PADGETT: Object to form.

THE WITNESS: -- literature, no. But I'm not aware of the concept of, you know, there could be conflicts if the study is directly relevant to a drug that that company is selling and it's a human clinical trial.

BY MS. HUNT:

Q Okay. I'd like to look at what has been marked as Exhibit 234.

Sorry for making you reach, Dr. Powell.

THE WITNESS: Oh, please, I wasn't complaining.

MR. PADGETT: But not me.

MS. HUNT: Bill, you're used to it.

(Powell Deposition Exhibit 234 marked for identification.)

BY MS. HUNT:

Q Okay. So does it appear to you that the title of this article is: "The disinformation playbook: How industry manipulates the science-policy process and how to restore scientific integrity."

Did I read that correctly?

A You did. That's the title of this article that

I've never read.

Q Moving down to footnote 1.

Do you know who the Union of Concerned Scientists are?

A No, I could guess, but no.

Q Okay.

A Never heard of them.

Q All right. I'd like to take a look at the abstract.

It says: "For decades, corporate undermining of scientific consensus has eroded the scientific process worldwide. Guardrails for protecting science-informed processes from peer-reviewed to regulatory decision-making have suffered sustained attacks, damaging public trust in the scientific enterprise and its aim to serve the public good. Government efforts to address corporate attacks have been inadequate. Researchers have cataloged corporate malfeasance that harmed people's health across diverse industries. Well-known cases like the tobacco industry's efforts to downplay the dangers of smoking are representative of transnational industries rather than unique. This contribution schematizes" -- I don't know, you might have to help me out with that, Dr. Powell -- "industry tactics to distort, delay, or distract the public from instituting measures that improve health. Tactics that

compromise the disinformation playbook."

Did I read that reasonably correctly?

A I would say that you read the words correctly, and I would ask to make sure that you didn't represent this paper as scientific research because if I said something about, yes, this is a scientific research study, it doesn't appear to me to be a research study. It appears to me to be either an opinion piece and/or an overview or review, just to be clear.

I don't remember what you asked me about this paper before, but I just wanted to make sure I didn't answer it incorrectly.

Q All right. I'd like to move to 234.3. And I want to take a look at Figure 1 up at the top here.

And it says here that the first step in the disinformation playbook is to fake the science. Do you see that in the second column?

And I know it's a little bit small and hard to read, so I'll read it for you.

A I can read it.

Q Okay. It says: "Conduct or fund counterfeit science and disguise it as legitimate research. Example, the maker of asbestos-containing baby powder, Johnson & Johnson, knowingly failed to use a testing method with adequate sensitivity to find asbestos levels and hid

unfavorable test results from the FDA."

Did I read that correctly?

MR. PADGETT: Object to form.

THE WITNESS: That's what it says.

BY MS. HUNT:

Q Okay. And then as we continue, it says: "Spread baseless or false doubt about the harm."

Then it says -- under step 2: "The scientific community speaks out."

It says: "Retaliate against scientists whose views, statements, or research is inconvenient for industry interests."

Let me ask you this: If Johnson & Johnson were to retaliate against scientists who have studied the link between acetaminophen and neurodevelopmental disorders; is that something that you would have a problem with?

MR. PADGETT: Object to form.

THE WITNESS: I think the -- I probably wouldn't have an opinion on that personally, but I'm sure other people might have a problem with it, other -- you know, federal government agencies, that sort of thing, FDA.

So I don't know the answer. I mean, it's -- me personally, I wouldn't pay much attention to it, frankly, unless it had to do with my practice.

I don't prescribe anything -- I don't prescribe baby powder and/or tanning, and I would have to say I'm aware of the Monsanto issues around, what is it, Roundup? Yeah, I've used Roundup.

So that -- that would bother me. That one bothers me, but the other stuff, I don't know.

BY MS. HUNT:

Q So as long as it doesn't affect you personally, you don't have an opinion on it one way or another?

MR. PADGETT: Object to form.

THE WITNESS: Well, that's not what I said.

But what I'm saying is, I don't prescribe baby powder or indoor tanning, and I said I use Monsanto.

So insofar as I use Roundup and other products in my daily life, it would concern me more than something that is outside of my realm of experience, which is prescribing baby powder, indoor tanning. I don't do that.

I mean, that's all I have to say.

BY MS. HUNT:

Q Are you aware that Johnson & Johnson has personally sued researchers in federal court for defamation over their findings that there's asbestos in baby powder?

A No.

MR. PADGETT: Object to form.
BY MS. HUNT:
Q Does that concern you at all?
A Does what concern me? The fact that --
MR. PADGETT: Same objection.
THE WITNESS: What's the concern? Does what concern me? Sorry.
BY MS. HUNT:
Q Does it concern you that this company, who you're serving as a paid expert for, would retaliate against scientists who found unfavorable results in their studies on Johnson & Johnson products?
MR. PADGETT: Object to form.
THE WITNESS: I can't be concerned about something that I'm unaware of.
BY MS. HUNT:
Q Okay. If it were true, is that something that would concern you?
MR. PADGETT: Same objection.
THE WITNESS: Concern me, I mean, yeah. It's concerning if it were true, and I don't know the basis of that and, you know, or the literature, so I really don't think it's valid for me to answer that question.
BY MS. HUNT:
Q Okay. And if you look below the figure, there's

this -- there's a section header that says: "Faking Science. Conducting or paying others to conduct flawed or bias scientific studies or hiding research with unfavorable conclusions."

And then it continues: "Industry-sponsored research is more likely to have favorable outcomes for the target product or process than research funded by other sources, a phenomenon known as the funding effect."

And then it continues: "Companies can publish studies with flawed methodologies, hire firms from the product defense industry, and publish ghostwritten articles." Those are just some examples from that list.

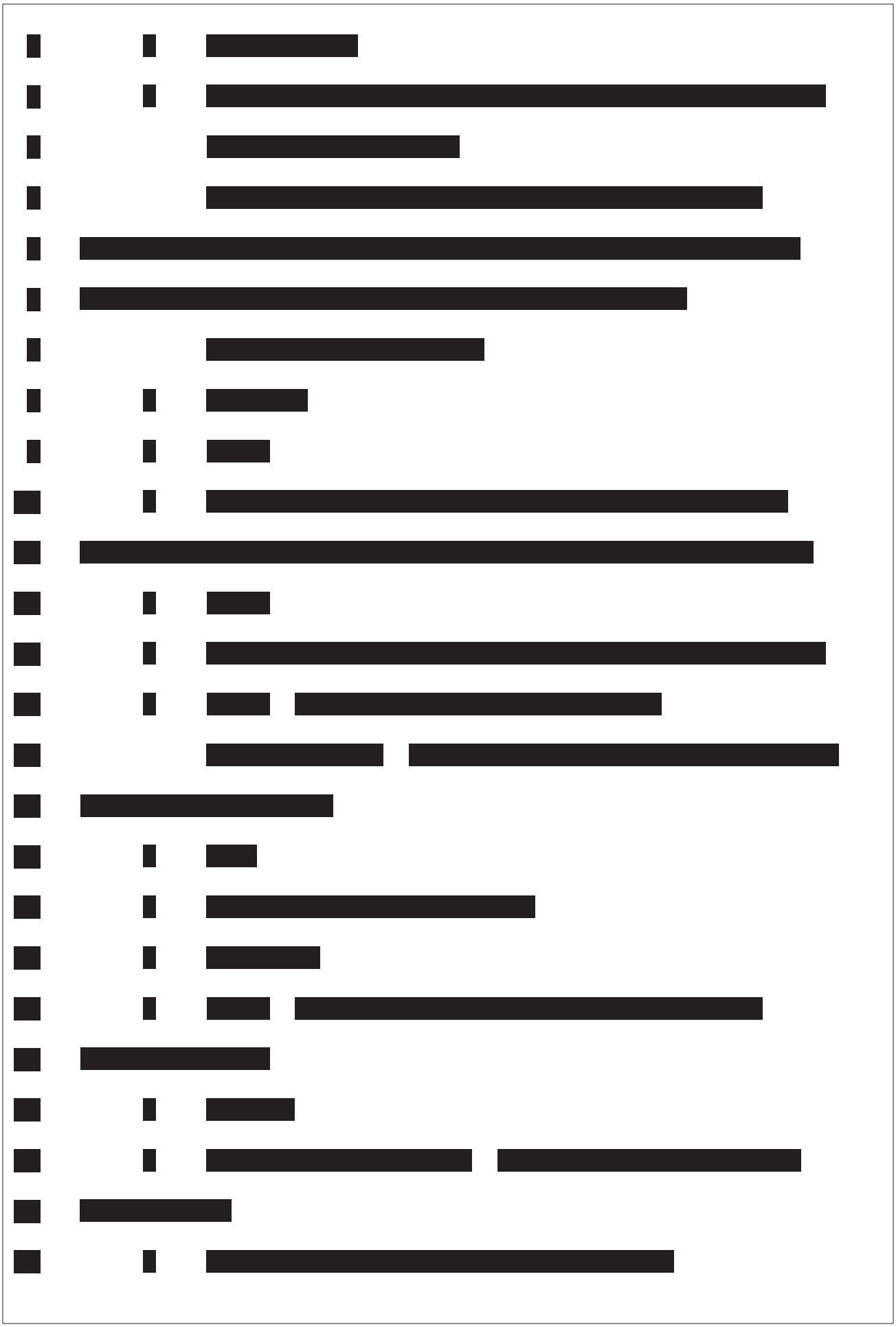
Are you aware of Johnson & Johnson doing any of those things related to acetaminophen in this case?

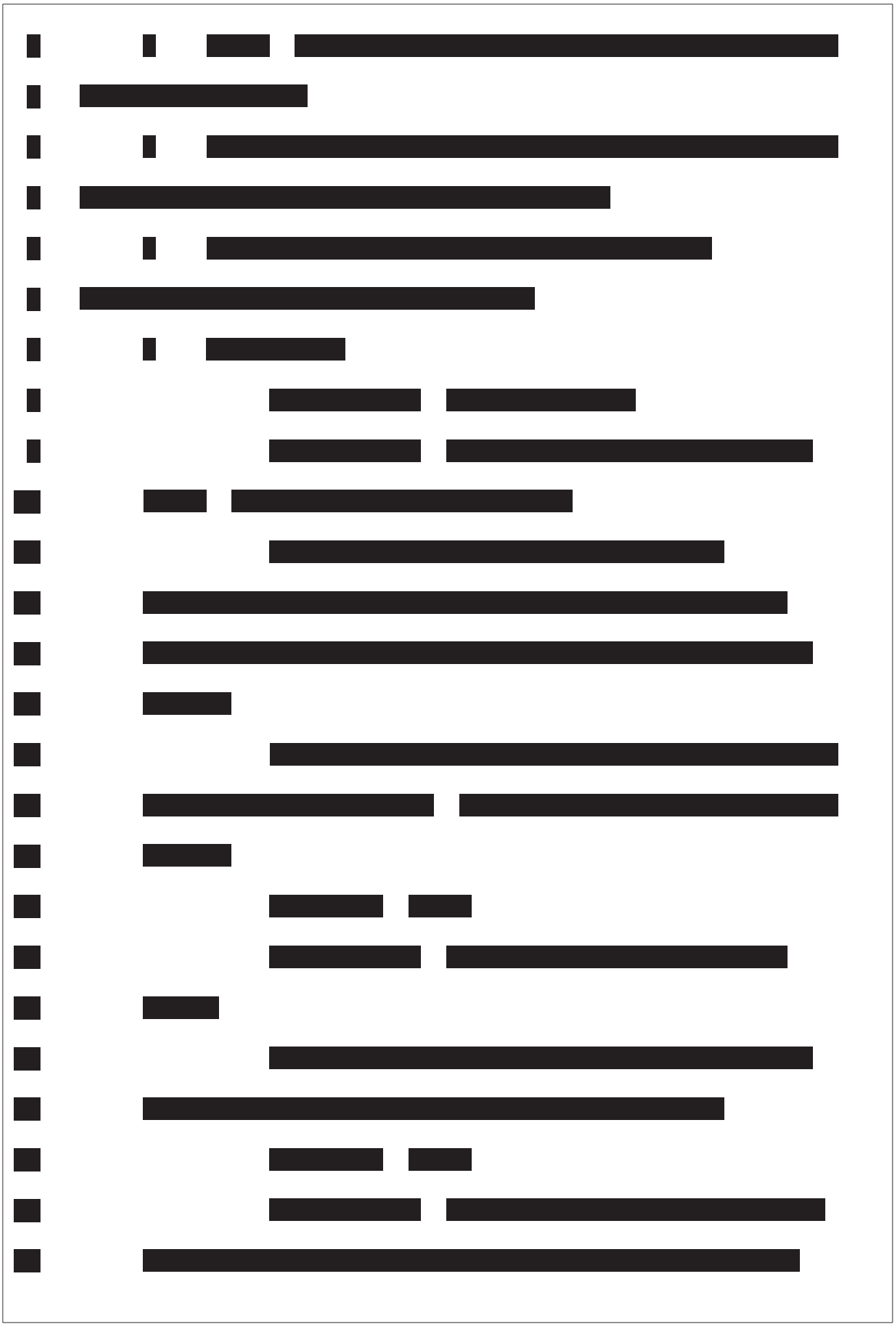
MR. PADGETT: Object to form.

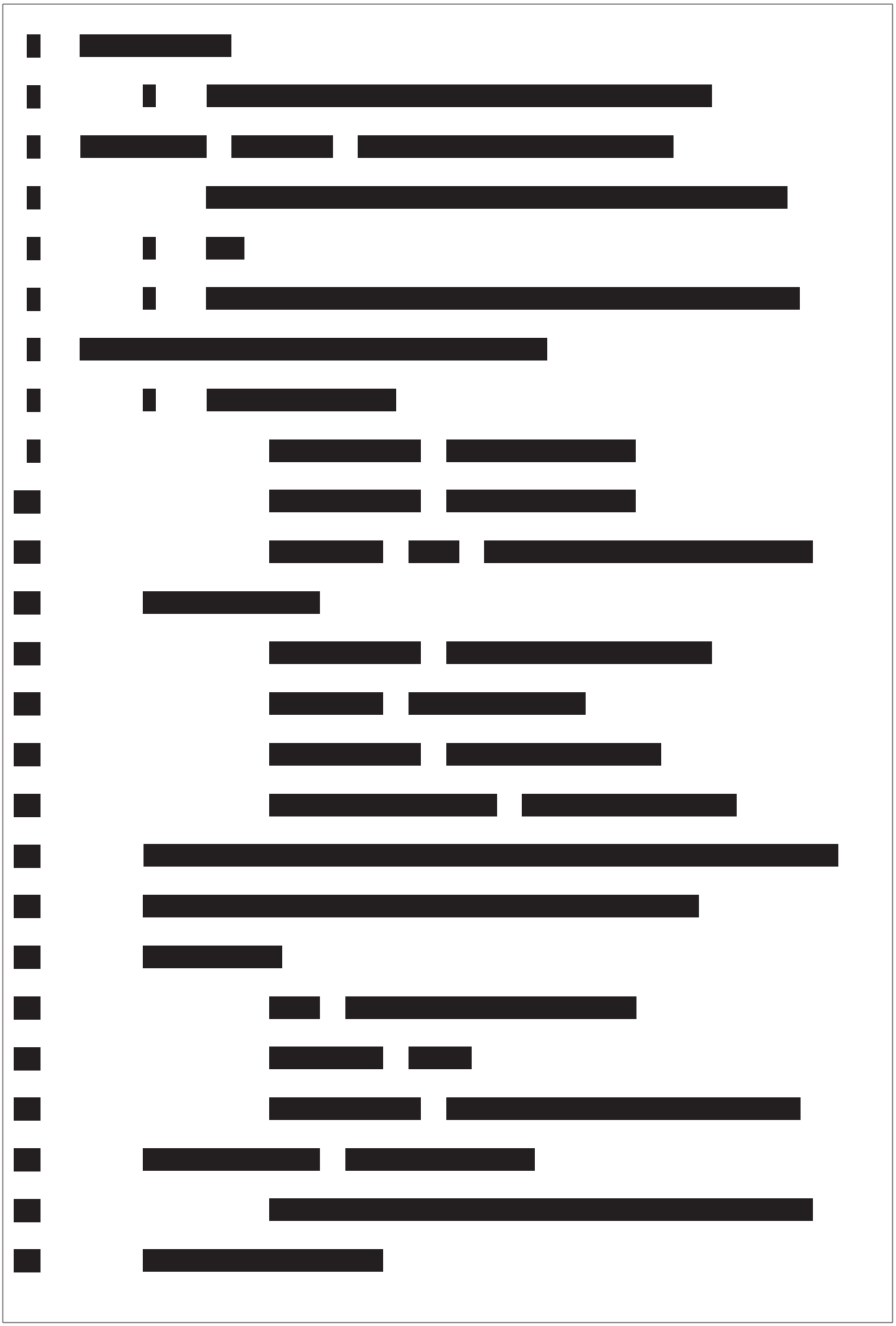
THE WITNESS: I don't -- no.

BY MS. HUNT:

[redacted]







[redacted]

BY MS. HUNT:

Q Okay. Are you aware that experts contacted by the plaintiffs in this case have been told by their institutions that they can't testify for fear of financial repercussions in terms of Johnson & Johnson pulling funding from their universities?

MR. PADGETT: Object to form.

THE WITNESS: I have no knowledge of that.

BY MS. HUNT:

Q Did you read the deposition of Dr. Cabrera?

A I believe I did, yes.

Q Do you know who Dr. Finnell is?

A No.

Q Dr. Rick Finnell at Baylor?

A No.

Q Doesn't ring a bell?

A I don't -- I don't think so. Rick Finnell at Baylor College of Medicine.

And what does he do here?

Q He's the reason we have fully interbred. He runs the lab there.

A Yeah, I don't know him.
Q Okay. So you're not aware of the testimony that he was not permitted to testify as an expert in this case for fear that Johnson & Johnson would seek retribution with Baylor?
MR. PADGETT: Object to form.
THE WITNESS: I don't recall that in a deposition, and so I'm not aware and wasn't aware.
BY MS. HUNT:
Q Are you aware of the testimony from Rachel Weinstein, the director of consumer epidemiology at Johnson Consumer, Inc., that she is part of an effort to publish pharmaceutical industry funded studies on acetaminophen?
MR. PADGETT: Object to form.
THE WITNESS: I have no knowledge of any of that.
BY MS. HUNT:
Q Okay. Did you ask to see any of the corporate depositions in this case?
A No.
Q Were you interested to see them?
MR. PADGETT: Object to form.
THE WITNESS: I'm not sure I had any idea they even existed when I was writing this report, and in preparing for the deposition, I guess I saw

references to the depositions and the other experts' reports, so to the extent that I -- not reports, but -- well, maybe the reports and/or the depositions, I think, I was aware that maybe that had happened based on that, but it was not primary information that I was aware of, other than through depositions and, you know, there's never a complete explanation of what's happened before in those depositions, so I don't really know what's happened.

BY MS. HUNT:

Q Okay. Do you think that the studies and the review papers that Johnson & Johnson Consumer, Inc., is funding are going to be objective?

MR. PADGETT: Object to form.

THE WITNESS: I would hope so.

BY MS. HUNT:

Q Are you aware that Johnson & Johnson Consumer, Inc., and other retailers who sell acetaminophen, sent process servers to the homes of scientists who have published on acetaminophen?

A No.

MR. PADGETT: Object to form.

BY MS. HUNT:

Q Are you aware that they were subpoenaed in federal court because of their publications about acetaminophen?

MR. PADGETT: Same objection.

THE WITNESS: Because of their what?

BY MS. HUNT:

Q Because of their published -- publications on acetaminophen?

A I have no knowledge of that.

Q Okay. And is it fair to say that none of this troubles you as a scientist?

A Well --

MR. PADGETT: Object to form.

THE WITNESS: What I don't know hasn't troubled me.

MS. HUNT: Can I take a quick break?

THE VIDEOGRAPHER: Off record, 5:14.

(Off the record at 5:14 p.m.)

THE VIDEOGRAPHER: On record, 5:27 p.m.

MS. HUNT: Dr. Powell, I have no more questions at this time. I'd like to reserve the remainder of my time for recross, if any.

MR. PADGETT: No questions.

THE VIDEOGRAPHER: Off record. 5:27 p.m.

(Deposition concluded at 5:27 p.m.)

– – –

CERTIFICATE

I, Jennifer A. Dunn, Registered Merit Reporter, Certified Realtime Reporter, Certified Shorthand Reporter, and Certified Court Reporter, do hereby certify that prior to the commencement of the examination, CRAIG POWELL, M.D., Ph.D., was duly remotely sworn by me to testify to the truth, the whole truth and nothing but the truth.

I DO FURTHER CERTIFY that the foregoing is a verbatim transcript of the testimony as taken stenographically by me at the time, place and on the date hereinbefore set forth.

I DO FURTHER CERTIFY that I am neither a relative nor employee nor attorney nor counsel of any of the parties to this action, and that I am neither a relative nor employee of such attorney or counsel, and that I am not financially interested in the action.

"/s/JENNIFER A. DUNN"

Registered Merit Reporter

Certified Realtime Reporter

Dated: August 31, 2023

INSTRUCTIONS TO WITNESS

Please read your deposition over carefully and make any necessary corrections. You should state the reason in the appropriate space on the errata sheet for any corrections that are made.

After doing so, please sign the errata sheet and date it. You are signing same subject to the changes you have noted on the errata sheet, which will be attached to your deposition.

It is imperative that you return the original errata sheet to the deposing attorney within thirty (30) days of receipt of the deposition transcript by you.

If you fail to do so, the deposition transcript may be deemed to be accurate and may be used in court.

ACKNOWLEDGMENT OF DEPONENT

I, CRAIG POWELL, M.D., Ph.D., do hereby certify that I have read the foregoing pages and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

_____

CRAIG POWELL, M.D., Ph.D. DATE

(Reported by: Jennifer A. Dunn, RMR, CRR, CCR & CSR)

Subscribed and sworn to before me this

_____ day of _____, 20 _____.

My commission expires: _____

_____

Notary Public

ERRATA SHEET

WITNESS: Craig Powell, M.D., Ph.D.

IN RE: Acetaminophen (Tylenol) ASD-ADHD Products Liability Litigation MDL No. 3043

Upon reading the deposition and before subscribing thereto, the deponent indicated the following changes should be made:

PAGE	LINE	CHANGE/REASON
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